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THE

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ORIGINAL ARTICLES

NEPHRITIC HYPERTENSION: CLINICAL AND EXPERIMENTAL STUDIES.[1]

By Theodore C. Janeway, M.D.,

Bard Professor of the Practice of Medicine, College of Physicians and Surgeons, Columbia University; Visiting Physician to the Presbyterian Hospital, New York City.

When Richard Bright,[2] in 1836, published his "Cases and Observations Illustrative of Renal Disease Accompanied with the Secretion of Albuminous Urine," he set in motion an inquiry that has been unrestingly pursued during the past three-quarters of a century, and that is today still far from its goal. This inquiry concerns the phenomenon of high arterial pressure in man and its relation to chronic disease of the kidneys. In this now famous paper, Bright gave the results of his clinical study of one hundred patients, compared with the findings at autopsy. His study revealed a coincidence of cardiac and renal disease so striking as to convince him that the disease of the heart must be regarded as the result, more or less direct, of the disease of the kidneys. He comments upon the relationship in these words:

"The deviations from health in the heart are well worthy of observation: they have been so frequent, as to shew a most important and intimate connection with the disease of which we are treating; while at the same time there have been twenty-seven cases in which no disease could be detected; and six others, which,

[1] Read before the Harvey Society, New York, February 15, 1913, and the Rush Society, Philadelphia, March 14, 1913.

[2] Cases and Observations Illustrative of Renal Disease Accompanied with the Secretion of Albuminous Urine, Guy's Hospital Report, London, 1836, i, 338.

from not having been noted, lead to the belief that no important deviation from the normal state existed. The obvious structural changes in the heart have consisted chiefly of hypertrophy, with or without valvular disease: and, what is most striking, out of fifty-two cases of hypertrophy, no valvular disease whatsoever could be detected in thirty-four: . . . This naturally leads us to look for some less local cause, for the unusual efforts to which the heart has been impelled: and the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately; or, that it so affects the minute and capillary circulation, as to render greater action necessary to force the blood through the distant subdivisions of the vascular system."

I ask you to note particularly two things: (1) While Bright was convinced that he had discovered a real relationship between pathologic processes in distant organs, he made no attempt to blink the fact that this relationship is by no means a constant one; (2) he did not speculate beyond certain broad inferences which, to his sane and clinically trained mind, seemed warranted by the facts themselves. These inferences were, that the hypertrophy of the heart must be attributed to unusual work performed by that organ, and that the cause of the unusual work must lie either in unwonted, direct stimulation of the heart or in heightened peripheral resistance. Either condition, it seemed to him, could be attributed to an altered quality of the blood, associated with the disease in the kidneys. That these suggestions contained the germ of such subsequent explanations of the phenomena as have attained to any wide acceptance, bears witness to the insight into disease processes which may be gained by the attentive study of clinical symptoms in connection with the concomitant anatomical lesions. It is an insight which in the history of medicine has usually recognized its own limitations. The contrast between such modes of thought and some of the more recent speculations on the same subject is apparent.

I. Theories and Experiments. For fifty years after Bright the origin of the cardiac hypertrophy found in kidney disease was a favorite theme of pathologists. It was the subject of extensive anatomic investigations and considerable experimental study. With the invention of the first clinical instrument for measuring blood pressure, by von Basch in 1876, the way was opened for fuller investigation of the physiology of the circulatory disorder of which the pathologist saw the end result. Since reasonably accurate instruments were brought forward in 1896 by Riva-Rocci and by Hill and Barnard, and the sphygmomanometer has been generally adopted in medical practice, the point of attack on the problem has shifted, so that at the centre of our inquiries today stands nephritic hypertension.

These two problems of nephritis, the cause of the high blood pressure and the cause of the hypertrophied heart, must not be identified absolutely. In the main, however, the hypertrophied heart may be looked upon as the result of a persistently high blood pressure. To this point of view practically all authorities are now committed. The evidence for this statement is well formulated by Krehl[3] and by Jores.[4] Such ideas as those of von Bühl,[5] that the hypertrophy is dependent upon inflammatory processes in the heart itself, have never had wide acceptance. Even Senator,[6] who in 1902 laid some stress on the first suggestion of Bright, that is, primary stimulation of the heart, as a factor at least in the hypertrophy found in so-called chronic parenchymatous nephritis, did not recur to this point of view in his last review of the subject.[7] Schlayer[8] has reported a few instances in which cardiac hypertrophy apparently preceded a rise in pressure. I, too, have seen young people in whom the heart seemed enlarged while the blood pressure remained within normal limits. In the normal animal, with intact vagus and vasomotor mechanisms, a long maintained high blood pressure is prevented automatically. It is also a common clinical observation that high arterial pressure persists even in patients with markedly incompetent hearts, the condition called by Sahli "Hochdruckstauung." I[9] have always been convinced, therefore, that the hypertrophy of the heart cannot explain the high blood pressure of nephritis, though it may be one contributing element. Krehl,[10] in the last edition of his book, also insists on this. Hence, I shall confine the present discussion of the problem to nephritic hypertension, using the word "nephritic" for the sake of brevity, not in any strict sense, but to indicate only association with disease of the kidneys. Until pathologists can all agree upon the diseases of the kidney which they will consider inflammatory and entitled to the designation "nephritis," clinicians may be pardoned for saving the time of their audiences by a loose use of terms.

While I shall present mainly the results of the newer clinical and experimental studies upon the subject, due weight must be given to the mass of anatomic evidence as to the relative frequency

[3] Pathologische Physiologie, Leipsic, 1912, 7th edition, pp. 36 and 37.

[4] Ueber die Beziehungen der Schrumpfnieren zur Herzhypertrophie vom pathologisch-anatomischen Standpunkt, Verhandl. deutsch. path. Gesellsch., 1908, xii, 187 (see editorial, Jour. Amer. Med. Assoc., 1909, lii, 565); Deutsch. Arch. f. klin. Med., 1908, xciv, 1.

[5] Ueber Bright's Granularschwund der Nieren und die damit zusammenhängende Herzhypertrophie, Mitteil. aus dem Path. Institut zu München, 1878, p. 38.

[6] Die Erkrankungen der Nieren, Vienna, 1902, pp. 110–129.

[7] H. Senator, Ueber die Beziehungen des Nierenkreislaufs zum arteriellen Blutdruck und über die Ursachen der Herzhypertrophie bei Nierenkrankheiten, Zeitschr. f. klin. Med., 1911, lxii, 189.

[8] Untersuchungen über die Funktion kranker Nieren, Deutsch. Arch. f. klin. Med., 1911, cii, 3 and 4, 323.

[9] Theodore C. Janeway, The Clinical Study of Blood Pressure, New York, 1904, p. 142.

[10] Pathologische Physiologie, Leipsic, 1912, 7th edition, p. 37.

of cardiac hypertrophy in the various types of nephritis. A theory of nephritic hypertension must be adequate to explain the underlying anatomic facts as well as the varied behavior of the blood pressure during life, including its response to therapeutic measures. It must be in accord with the recognized physiologic laws governing the circulation. The problem, however, is set by the clinical facts, and it should be borne in mind that permanent hypertension is a human pathologic phenomenon, which has no counterpart in the realm of normal animal physiology thus far investigated.

Mechanical Theories. The only theory which has sought to explain the hypertension of nephritis on different lines from those suggested by Bright has been the purely mechanical theory first advocated by Traube[11] and elaborated by Cohnheim.[12] In its original form it sought to explain high pressure by increased peripheral resistance in the kidney itself. This theory was disproved by the observation that ligature of both renal arteries fails to raise the blood pressure. It has recently been resurrected in modified form by Katzenstein,[13] who claimed to get a slight rise in blood pressure after incomplete occlusion of the renal vessels and after temporary complete occlusion, by which he claimed to produce thrombosis of the smaller renal arteries. There was a rise in the blood pressure of the animal when the circulation was reëstablished. Further experiments in this direction, made by Müller and Maas,[14] who embolized the kidney extensively with paraffin, failed to demonstrate a rise in blood pressure. Alwens,[15] also, does not confirm Katzenstein's observations, but he was able to produce small rises in blood pressure by compressing the kidneys in oncometers, using an amount of external pressure approximating or surpassing the aortic blood pressure. The same amount of pressure applied to the lower extremities was without influence. Alwens himself admits that the rise in pressure obtained under these conditions is too slight, as compared with the hypertension of nephritis, to suggest that the mechanical factor is more than subordinate in the production of human high blood pressure. He admits also that the mechanism is purely passive, the actual transmission of the pressure exerted upon the kidney out through the renal artery to the aortic blood column. Such a procedure, as Senator[16] remarks, can have no counterpart in human pathology, where the only source of pressure available is the existing aortic blood pressure.

[11] Gesammelte Abhandlungen, Berlin, 1856, ii, 290; iii, 440.

[12] Vorlesungen über allgemeine Pathologie, Berlin, 1880, ii, 355.

[13] Experimenteller Beitrag zur Erkenntnis der bei Nephritis auftretenden Hypertrophie des linken Herzens, Virchow's Arch. f. path. Anat., 1905, clxxxii, 327.

[14] H. Senator, Ueber die Beziehungen des Nierenkreislaufs zum arteriellen Blutdruck und über die Ursachen der Herzhypertrophie bei Nierenkrankheiten, Zeitschr. f. klin. Med., 1911, lxii, 189.

[15] Experimentelle Untersuchungen über die Bedeutung der mechanischen Theorie der nephritischen Blutdrucksteigerung, Deutsch. Arch. f. klin. Med., 1910, xcviii, 137–163.

[16] Ueber die Beziehungen des Nierenkreislaufs zum arteriellen Blutdruck und über die Ursachen der Herzhypertrophie bei Nierenkrankheiten, Zeitschr. f. klin. Med., 1911, lxii, 189.

A theory which can in part be interpreted as mechanical was propounded by Loeb.[17] It was based upon the claim that the anatomic study of nephritics showing hypertension brought out a parallelism between the extent of glomerular changes and the height of the blood pressure. Upon this finding was based the theory that the hypertension of nephritis should be considered in the nature of a regulatory function, probably evoked reflexly, in order to provide an adequate flow of blood through the kidney, when local vasodilatation within that organ was no longer sufficient, because of capillary obliteration in the diseased glomeruli. The anatomic basis of Loeb's theory has been destroyed by Jores[18] in a careful study of serial sections taken from the kidneys of four subjects. The two who had shown the highest blood pressure and the most marked cardiac hypertrophy had the least extensive glomerular lesions. He also cited one instance where the heart was markedly hypertrophied and the kidneys showed scarcely recognizable histologic changes. Certainly no one who has had the opportunity to observe a large series of autopsies on nephritic individuals can fail to agree with Jores, that there is no strict parallelism between glomerular changes and blood pressure. While it seems clear that the types of nephritis most regularly characterized by hypertension are characterized equally by extensive glomerular lesions, it is also evident that there exist, as Bright observed and as all subsequent statistics have shown, many instances of extreme glomerular nephritis without cardiac hypertrophy.[19] The most fatal objection to a purely glomerular theory of hypertension lies in the fact that amyloid disease, which is *par excellence* a disease of the glomeruli, in its pure form is almost invariably without effect on the blood pressure, and without an accompanying hypertrophy of the heart. This fact is one of the most difficult to be reconciled with any theory of nephritic hypertension.

Chemical Theories. The germ of the many chemical theories, as we have seen, lies in Bright's suggestion that altered composition of the blood is the probable cause. Johnson[20] first elaborated

[17] Ueber Blutdruck und Herzhypertrophie bei Nephritikern, Deutsch. Arch. f. klin. Med., 1905, lxxxv, 348.

[18] Ueber die Beziehungen der Schrumpfnieren zur Herzhypertrophie vom pathologisch-anatomischen Standpunkt, Verhandl. deutsch. path. Gesellsch., 1908, xii, 187 (see editorial, Jour. Amer. Med. Assoc., 1909, lii, 565); Deutsch. Arch. f. klin. Med., 1908, xciv, 1.

[19] Von Bühl (Ueber Bright's Granularschwund der Nieren und die damit zusammenhängende Herzhypertrophie, Mitteilungen aus dem Path. Institut zu München, 1878, p. 57) extremely contracted kidneys without enlargement of the left ventricle, 7.9 per cent.; Potter (Cardiac Hypertrophy as Observed in Chronic Nephritis; Russell Sage Institute of Pathology Statistics, Jour. Amer. Med. Assoc., 1906, xlvii, 1354) 66 cases of chronic interstitial nephritis, no hypertrophy, 58 per cent. (a large number of these were in aged or greatly debilitated individuals, and the estimate of hypertrophy was not by Müller's method of weighing); von Bamberger (Ueber Morbus Brightii und seine Beziehungen zu anderen Krankheiten, Samml. klin. Vorträge, No. 173, September 3, 1879) 807 cases of primary Bright's disease, enlargement of the heart in 344, or 42.6 per cent.; Hirsch (Ueber die Beziehungen zwischen dem Herzmuskel und die Körpermuskulatur, und über sein Verhalten bei Herzhypertrophie, Deutsch. Arch. f. klin. Med., 1899, lxiv, 597; 1900, lxviii, 55, 321), weighing by Müller's method, small material, 72 per cent.

[20] The Pathology of the Contracted Granular Kidney, London, 1896.

this suggestion into the conception that accumulated waste products due to failure of the excretory function of the kidney cause vasomotor spasm and later hypertrophy of the muscular coats of the arteries. The older experimental work along this line gave inconclusive results. Excision of a single kidney was without clear-cut effects, and double nephrectomy led to too rapid death for cardiac hypertrophy to develop. Recent experiments by Mosler,[21] in which thirteen rabbits survived the removal of both kidneys for forty-eight hours, showed a rise in the carotid blood pressure of all the animals but two, the rise being over 15 mm. in four and 25 mm. in one. Real insight into the problem of the complex changes accompanying quantitative renal insufficiency was first afforded by the admirable studies of Tuffier,[22] and especially of Rose Bradford.[23] The latter excised one kidney in a large series of dogs, and watched the effect of removing successive portions of the remaining kidney. Bradford discovered that the removal of three-quarters of the total kidney substance resulted in death by emaciation and asthenia in from one to six weeks. The removal of two-thirds often resulted similarly; but if less than two-thirds were taken out, the animal showed practically no serious disturbances. His findings have been corroborated by Pearce[24] and his coworkers, who have improved upon the methods and have made valuable studies of nitrogen metabolism in such animals. Pearce occasionally was able to remove even three-quarters of the kidney substance in dogs without producing serious symptoms. It is clear then that for dogs the "factor of safety" in the kidney, in Meltzer's[25] sense, is approximately two-thirds, and the indispensable amount of kidney substance required by the animal not over one-third. Animals with these extreme reductions in kidney substance, which may be considered analogous to advanced kidney atrophy in man, developed early and marked polyuria.

In 1905 Pässler and Heineke[26] applied this method to the problem of hypertension. They argued that as high blood pressure is most common in individuals with contracted kidneys it was reasonable to suppose that some relation between blood pressure and amount of functioning kidney tissue would be disclosed. They performed successive reductions of kidney substance in 18 dogs, of which 7

[21] Ueber Blutdrucksteigerung nach doppelseitiger Nierenextirpation, Zeitschr. f. klin. Med. 1912, lxxiv, 297 to 302.

[22] Etudes expérimentelles sur la chirurgie des reins, Paris, 1889 (quoted by Rose Bradford).

[23] The Results Following Partial Nephrectomy and the Influence of the Kidney upon Metabolism, Jour. Phys., 1899, xxiii, 415.

[24] The Influence of the Reduction of Kidney Substance upon Nitrogenous Metabolism, Jour. Exp. Med., 1908, x, 632. A Study of Experimental Reduction of Kidney Tissue, with Special Reference to the Changes in that Remaining, Jour. Exp. Med., 1908, x, 745.

[25] The Factors of Safety in Animal Structure and Animal Economy, Harvey Lectures, Philadelphia, 1906–1907, p. 139.

[26] Versuche zur Pathologie des Morbus Brightii, Verhandl. d. deutsch. path. Gesellsch., 1905, ix, 99.

lived longer than four weeks without severe cachexia. On 5 of these dogs they made satisfactory blood-pressure observations by taking readings from the femoral artery before operation, eight days after operation, and several weeks after the last operation. These dogs showed an average increase in the blood pressure of 21.5 mm., the maximum increase being 29 and the minimum 15 mm. If too much tissue was removed a cachectic state ensued and the blood pressure fell. These 5 dogs also showed well-marked hypertrophy of the left ventricle as compared with the right. For all 7 dogs the average proportionate weight of the left ventricle to the right showed an increase over the normal of 28.5 per cent. These dogs quite regularly developed polyuria before the rise in blood pressure occurred. No reasonable criticism can be urged against these experiments. Pässler,[27] in a review of the whole subject, based on his experiments and clinical studies, concludes (1) that the hypertrophied heart in nephritis is the consequence of the kidney disease; (2) that as a result of the kidney lesion there probably occurs an increased irritability of the vasoconstrictor apparatus, in consequence of which arise arterial spasm and increase of resistance in the aortic circulation; (3) that the hypertrophy of the left auricle and of the right heart in nephritis is a later consequence of insufficiency of the left ventricle. This he argues not only from the finding of pure left ventricular hypertrophy in his experiments but from a critical review of the clinical evidence, which seems to me satisfying.

Formerly, hypertrophy of the entire heart, right as well as left, frequently found in the extensive postmortem statistics, seemed a serious obstacle to the acceptance of any theory which sought to explain the hypertrophy on the basis of increased resistance in the aortic circulation. Krehl, in the earlier editions of his *Pathologische Physiologie*, was strongly impressed with the difficulty of explaining this right ventricular hypertrophy. Many attempts were made to discover factors which would influence equally the right and the left heart. Increased viscosity of the blood, for instance, was postulated until clinical studies showed that this did not usually exist in hypertensive nephritis.[28] There is a small but interesting group of patients in whom polycythemia and chronic hypertension are associated, the so-called polycythemia hypertonica of Geisböck.[29] These cases differ from ordinary polycythemia in the absence of an enlarged spleen. That increased viscosity in itself cannot explain hypertension is clear, however,

[27] Ueber Ursache und Bedeutung der Herzaffektion Nierenkranker, Samml. klin. Vorträge, 1906, No. 408 (Serie xiv, 18), Inn. Med., No. 123, p. 525.

[28] C. Hirsch and Carl Beck, Studien zur Lehre von der Viscosität (inneren Reibung) des lebenden menschlichen Blutes, Deutsch. Arch. f. klin. Med., 1902, lxxii, 560.

[29] Die praktische Bedeutung der Blutdruckmessung, Verhandl. d. Kong. f. inn. Med., 1904, xxi, 97. Die Bedeutung der Blutdruckmessung f. die Praxis, Deutsch. Arch. f. klin. Med., 1905, lxxxiii, 363.

from such an example as that reported by Lommel.[30] In his patient, extreme polycythemia was unassociated with rise in blood pressure during life or hypertrophy of the heart at autopsy. Lucas[31] has recently reviewed 189 cases of erythremia and finds that hypertension existed in only a third.

Changes in the right heart are most often lacking in young persons dying accidentally or without a long illness. I have seen exquisite concentric hypertrophy of the left ventricle alone in a girl of sixteen, with extremely contracted kidneys, who died in uremic convulsions. The weighings of Hirsch[32] by Müller's method have shown that the usual sequence of events is (1) hypertrophy of the left ventricle, (2) later in the disease the development of disturbances of compensation, (3) then consecutive hypertrophy of the right ventricle. That another factor may perhaps be involved is suggested by Stewart's[33] study of cardiac hypertrophy resulting from the artificial production of aortic insufficiency in dogs, a purely mechanical lesion. All the chambers of the heart in his animals showed some increase in weight, though the increase was by far the greatest for the left ventricle.

In 1908–1909, with the assistance of Carrel, I attempted to study more in detail the increase in blood pressure following reduction of kidney substance.[34] As it is not possible to take innumerable blood-pressure readings directly from an artery, I devised a modified Riva-Rocci method,[35] by means of which I was enabled to take approximate readings from the foreleg of the dog. The blood pressure was studied in twenty-three dogs. On ten an operation for the excision of one kidney was made, with infarction of a considerable portion of the remaining kidney by ligature of branches of the renal artery at the hilum. Some of the animals were lost because of too extreme reduction of kidney substance and from accidental causes. One dog (No. 19) survived the operation thirty-nine days; he did well for twenty-one days, but then went into a state of progressive cachexia, with gastro-intestinal disturbances, as described by Bradford[36] and by Pearce.[37] The blood pressure

[30] Ueber Polycythaemia mit Milztumor, Deutsch. Arch. f. klin. Med., 1906, lxxxvii, 338.

[31] Erythremia or Polycythemia, with Chronic Cyanosis and Splenomegaly, Arch. Int. Med., 1912, x, 597.

[32] Ueber die Beziehungen zwischen dem Herzmuskel und die Körpermuskulatur, und über sein Verhalten bei Herzhypertrophien, Deutsch. Arch. f. klin. Med., 1899, lxiv, 597.

[33] An Experimental Contribution to the Study of Cardiac Hypertrophy, Jour. Exp. Med., 1911, xiii, 187.

[34] Theodore C. Janeway, Note on the Blood-pressure Changes Following Reduction of the Renal Arterial Circulation, Proc. Soc. Exp. Biol. and Med., 1909, vi, 109 to 111.

[35] Theodore C. Janeway, A Modification of the Riva-Rocci Method of Determining Blood-Pressure for Use on the Dog, Proc. Soc. Exp. Biol. and Med., 1909, vi, 108.

[36] The Results following Partial Nephrectomy and the Influence of the Kidney upon Metabolism, Jour. Phys., 1899, xxiii, 415.

[37] The Influence of the Reduction of Kidney Substance upon Nitrogenous Metabolism, Jour. Exp. Med., 1908, x, 632. A Study of Experimental Reduction of Kidney Tissue, with Special Reference to the Changes in that Remaining, Jour. Exp. Med., 1908, x, 745.

which had averaged 106 mm. before operation and 127 mm. during the first twenty-one days, fell to an average of 83 during the terminal illness.

BLOOD-PRESSURE READINGS IN MILLIMETERS ON DOG NO. 19.

	Maximum.	Minimum.	Average.
Before operation, 15 days, 4 readings	110	100	106
After operation, 21 days, 7 readings	135	120	127
Terminal period, 14 days, 3 readings	110	70	83

The above is analogous to what one sees occasionally when human beings with high pressure develop a terminal infection or wasting disease. Two dogs showed unequivocal, sustained hypertension; they were followed for 104 and 163 days respectively. Polyuria was evident, as in former experiments of this type. Albumin was usually present in the urine, which Pearce[38] has suggested evidenced nephritis in the remaining functioning kidney; but except in the neighborhood of the infarct the histologic appearances were normal.

BLOOD-PRESSURE READINGS IN MILLIMETERS ON DOG NO. 12.

	Maximum.	Minimum.	Average.
Before operation, 45 days, 7 readings	110	80	90
After operation, first 28 days, 8 readings	120	100	111
After operation, second 28 days, 10 readings	140	110	119
After operation, third 28 days, 11 readings	150	110	121
After operation, fourth 28 days, 12 readings	140	110	126
After operation, fifth 28 days, 7 readings	130	115	120
After operation, final 23 days, 7 readings	145	120	134

BLOOD-PRESSURE READINGS IN MILLIMETERS ON DOG NO. 20.

	Maximum.	Minimum.	Average.
Before operation, 23 days, 11 readings	135	95	117
After operation, first 28 days, 13 readings	175	130	157
After operation, second 28 days, 15 readings	165	130	150
After operation, third 28 days, 6 readings	185	150	158
After operation, fourth 20 days, 6 readings	165	150	156

These experiments, it seems to me, confirm and extend the results obtained by Pässler and Heineke.[39] They have not the same validity as a demonstration of the effect of purely quantitative reduction of kidney substance, as the infarcted portion of kidney was left *in situ*. It might be argued that the high blood pressure was the result of absorption of the products of disintegration of kidney tissue in the infarcted area, but the duration of the high blood pressure for weeks after the infarct was converted into a mass of partly calcified fibrous tissue would seem to make this criticism negligible.

[38] The Problem of Experimental Nephritis, Harvey Lectures, Philadelphia, 1909–10, p. 55.

[39] Versuche zur Pathologie des Morbus Brightii, Verhandl. d. deutsch. path. Gesellsch., 1905, x, 99.

From the standpoint of the dog, therefore, it seems clear, as Pässler and Heineke have shown, that moderate hypertension follows the quantitative reduction of kidney tissue to about a third of the total. My experiments show that such hypertension may be maintained for a long period. The rise in blood pressure thus produced is therefore more analogous to the hypertension of chronic nephritis in man than the transient hypertension of most animal experiments dealing with this problem. By what mechanism this increased blood pressure is brought about is wholly obscure, but that it must be associated, as Pässler[40] predicates, with increased tonus of the systemic arteries seems inescapable.

RENIN. Many attempts have been made to discover chemical substances exerting a pressor effect which could be conceived as accumulating in the blood in kidney disease. Simple retention of urea or other metabolites failed to accord with the facts. In 1898 Tigerstedt and Bergman[41] extracted from the rabbit's kidney a substance which they called renin and which, when injected into animals produced a rise of blood pressure. H. Batty Shaw[42] reviewed this subject extensively in the Goulstonian lectures for 1906, and advocated with enthusiasm the theory of autolysis of the kidney, with liberation of some pressor substance of this type, as the explanation of nephritic hypertension. Bingel and Strauss[43] have confirmed the pressor effects of renin. More recently, Pearce[44] has investigated the effects of kidney extracts from various animals on the same and other animal species, with altogether variable results. For instance the extract of dog kidney injected into the dog caused a decided fall in blood pressure; the same was true of rabbit's extract; while rabbit kidney and dog kidney extracts injected into the rabbit produced a slight rise. J. L. and E. M. Miller[45] have failed to obtain pressor effects from saline extracts of kidney or of any other organ except the spleen, hypophysis, and adrenal. It is, moreover, an acknowledged clinical fact that hypertension is most extreme in those exquisitely chronic types of nephritis in which the breaking down of kidney substance must be at a minimum if there is any at all. This fact, to my mind, so argues against the hypotheses that have been cited that I think it is reasonable to dismiss them from consideration.

EPINEPHRIN. The search for a chemical principle within the body by which to explain the phenomenon of increased blood

[40] Ueber Ursache und Bedeutung der Herzaffektion Nierenkranker, Samml. klin. Vorträge, 1906, No. 408 (Serie xiv, 18), Inn. Med., No. 123, p. 525.

[41] Niere und Kreislauf, Skand. Arch. f. Physiol., 1898, viii, 223.

[42] Auto-intoxication: its Relation to Certain Disturbance of Blood Pressure, 1906, Lancet, i, 1295, 1375, 1455.

[43] Ueber die blutdrucksteigernde Substanz der Niere, Deutsch. Arch. f. klin. Med., 1909, xcvi, 476.

[44] An Experimental Study of the Influence of Kidney Extracts and of the Serum of Animals with Renal Lesions upon the Blood Pressure, Jour. Exp. Med., 1909, xi, 430.

[45] The Effect on Blood Pressure of Organ Extracts, Jour. Phys., 1911, xliii, 242.

pressure seemed to have attained its goal in Oliver and Schäfer's[46] discovery of the remarkable effects produced by extracts of the suprarenal gland. The development of the adrenalinemia theory of hypertension makes a fascinating chapter in the history of speculative medicine. It is so rich in lessons and belief in the theory is so widespread that I propose to sketch it in detail. The hypothesis that increased secretion of the suprarenals might be the long-sought cause of nephritic hypertension was first proposed by Neusser,[47] but merely as a shrewd guess, from a single clinical case of chronic Bright's disease with carcinoma of one adrenal. The first attempts to bring forward arguments in support of the assumption were made in France. Vaquez[48] in 1904, in a paper read before the French Congress of Medicine, produced some autopsy observations made by his pupils, Aubertin and Ambard, showing the presence of nodular hyperplasia of the suprarenals, and of actual adenomas in cases of hypertensive nephritis, and brought into line with them Josue's recent studies of the arterial lesions produced by epinephrin. This evidence was received with enthusiasm; but further anatomic investigations, particularly those of Landau,[49] Pearce,[50] Thomas,[51] and Borberg,[52] made on extensive material, have failed to show a constant relation between anatomic lesions of the adrenals and the hypertension of nephritis or arteriosclerosis. Similar suprarenal lesions have also been found in persons dying of other diseases. To a large extent it now seems probable that the changes found in the gland are the result of local arteriosclerosis of its own vessels rather than *vice versa*. The experimental lesions produced by epinephrin, moreover, are quite unlike human arteriosclerosis. Pearce[53] suggests that hyperplasia of the adrenal probably represents the effect of some factor operating in the later period of life, during which chronic nephritis and arterial affections are most frequent. The relations are evidently complicated and the anatomic evidence of excessive suprarenal function is unconvincing. Perhaps the most extensive work upon the subject is Ingier and Schmorl's[54] determination of the epinephrin content of the adrenals in 517 autopsies. They found an

[46] The Physiological Effects of Extracts of the Suprarenal Capsules, Jour. Phys., 1895, xviii, 231.

[47] Artur Biedl, Innere Sekretion, Berlin, 1910, p. 243.

[48] Hypertension, Proc. Congrès Français de Méd., 1904, p. 338.

[49] Ueber die anatomischen Veränderungen in den Nebennieren bei Arteriosklerose, Zeitschr. f. klin. Med., 1907, lxiv, 227.

[50] The Relation of Lesions of the Adrenal Gland to Chronic Nephritis and to Arteriosclerosis: an Anatomical Study, Jour. Exp. Med., 1908, x, 735.

[51] Ueber Veränderungen der Nebennieren, insbesondere bei Schrumpfnieren, Beiträge z. path. Anat. u. z. allgem. Path., 1910, xlix, 228.

[52] Das chromaffine Gewebe. Nebennierenuntersuchungen, Skand. Arch. f. Physiol., 1912, xxviii, 91 (abstract, Zentralbl. f. d. gesamm. inn. Med., 1913, iv, 383).

[53] The Relation of Lesions of the Adrenal Gland to Chronic Nephritis and to Arteriosclerosis: an Anatomical Study, Jour. Exp. Med., 1908, x, 735.

[54] Ueber den Adrenalingehalt der Nebennieren, Deutsch. Arch. f. klin. Med., 1911, civ, 262.

increase of epinephrin in the glands in acute nephritis, and in seventeen patients with chronic nephritis, with higher values on the average in those having high blood pressure and hypertrophied hearts. On the other hand their highest figure, almost three times the normal average, was from an individual without either an hypertrophied heart or arteriosclerosis; and the three next highest figures were from similar cases. Again, the subject with the greatest cardiac hypertrophy showed a far lower epinephrin content, actually less than the normal. These results can be more readily explained along the lines suggested by Pearce.[55]

The well-marked hypotension of Addison's disease and the rapid death with a sharp fall in blood pressure which followed the earlier extirpations of the adrenals were assumed to be the reverse side of the picture. To many minds the evidence of diminished adrenal secretion seemed so clear that the assumption of increased adrenal secretion as the cause of the opposite effect upon blood pressure and heart was an easy step. But the more the cause of death after removal of the adrenals has been studied and the better the operative technique employed, the further have the effects upon blood pressure receded into the background. Many investigators have now succeeded in extirpating the adrenals, or in excluding them from the circulation by ligature of their veins, without producing immediate effects upon blood pressure. After Hultgren and Andersson's[56] technically perfect removal of the adrenals the blood pressure in some of the animals remained normal for two or three days. In this country Hoskins and McClure[57] have recently performed similar experiments. They seem to me of crucial importance. The effect of epinephrin is so transient that, were the normal tonus of the bloodvessels dependent upon its presence, the exclusion of the suprarenals from the circulation must cause a prompt and unmistakable fall in blood pressure. Furthermore, there seems reason to believe that the cortex, not the medulla of the adrenal, is the structure essential to life. The cortex, as is well known, plays no part in the elaboration of epinephrin. The whole question is extensively discussed by Biedl[58] and by Bayer;[59] Biedl seems to lean toward this view. Plainly therefore the hypotension of Addison's disease can in nowise be used as an argument to bolster up the assumption that hypertension is an affair of hypersecretion of the adrenals.

With the increasing activity of physiologists in investigating the action of epinephrin, methods became available for its identifi-

[55] The Relation of Lesions of the Adrenal Gland to Chronic Nephritis and to Arteriosclerosis: an Anatomical Study, Jour. Exp. Med., 1908, x, 735.

[56] Artur Biedl, Innere Sekretion, Berlin, 1913, 2d edition, p. 373.

[57] The Relation of the Adrenal Glands to Blood Pressure, Amer. Jour. Phys., 1912, xxx, 192.

[58] Innere Sekretion, Berlin, 1913, 2d edition.

[59] Normale und pathologische Physiologie des chromaffinen Gewebes der Nebennieren, Ergebn. d. allg. Path. u. pathol. Anat., 1910, xiv, II, 1.

cation in exceedingly dilute solutions. Batelli[60] reported in 1902 that he obtained a pressor effect by injecting concentrated dog serum into rabbits which corresponded to an epinephrin concentration in the blood of 1 to 20,000,000. The first clinical work to attract widespread attention to the supposed presence of epinephrin in the circulating blood of nephritics was a publication by Schur and Wiesel.[61] Their test object was the excised eye of the frog, which dilates with epinephrin, a method first described by Meltzer.[62] They also claimed to identify epinephrin chemically by the ferric chloride reaction. Schur and Wiesel[63] prophesied that it would soon be proved that the high blood pressure, the cardiac hypertrophy, and the vascular changes of kidney disease are related to increased activity of the chromaffin system, which was at that time beginning to attract wide notice. Schlayer[64] promptly made tests by the Meyer artery strip method, using normal sera, and in ten experiments, nephritic sera from hypertensive patients. He found that normal serum, even after removal of the albumin, always contained a constrictor substance which resisted dialysis, was diminished by concentration *in vacuo*, and therefore resembled epinephrin. The nephritic sera in all but one case produced much less constriction than normal sera. He concluded therefore that Schur and Wiesel's results had no validity because they had been unable to identify an epinephrin-like substance in normal blood, and held that the hypothesis of a connection between nephritic hypertension and adrenal function was as yet unproved. Schlayer[65] made a number of other studies by the Meyer[66] method, and came to the conclusion that arteries would not react to epinephrin in any but homologous blood. Fraenkel[67] using the uterus suspension as a test object; Trendelenburg[68] using the frog perfusion preparation of Läwen;[69] and later Bröking and Trendelenburg,[70]

[60] Présence d'adrénaline dans le sang d'animaux. Son dosage, Comptes rendus de la Soc. de Biol., 1902, liv, 1179.

[61] Ueber eine der Adrenalinwirkung analoge Wirkung des Blutserums von Nephritikern auf das Froschauge, Wien. klin. Woch., 1907, xx, 699.

[62] The Effect of Suprarenal Extract upon the Pupils of Frogs, Amer. Jour. Phys., 1904, xi, 449.

[63] Zur Frage drucksteigernder Substanzen im Blute bei chronischer Nephritis, Deutsch. med. Woch., 1907, xxxiii, 2136.

[64] Zur Frage drucksteigernder Substanzen im Blute bei chronischer Nephritis, Deutsch. med. Woch., 1907, xxxiii, 1897.

[65] Zur Frage der blutdrucksteigernden Substanzen im Blute bei Nephritis, Münch. med. Woch., 1908, lv, 2604.

[66] Ueber einige Eigenschaften der Gefässmuskulatur, mit besonderer Berücksichtigung der Adrenalinwirkung, Zeitschr. f. Biol., 1906, xxx, 352.

[67] Ueber den Gehalt des Blutes an Adrenalin bei chronsicher Nephritis und Morbus Basedowii, Arch. f. exper. Path. u. Pharmakol., 1909, lx, 395.

[68] Bestimmung des Adrenalingehaltes im normalen Blut, sowie beim Abklingen der Wirkung einer einmaligen intravenösen Adrenalininjektion mittels physiologischer Messmethode, Arch. f. exper. Path. u. Pharmakol., 1910, lxiii, 161.

[69] Quantitative Untersuchungen über die Gefässwirkung von Suprarenin, Arch. f. exper. Path. u. Pharmakol., 1904, li, 415.

[70] Adrenalinnachweis und Adrenalingehalt des menschlichen Blutes, Deutsch. Arch. f. klin. Med., 1911, ciii, 168.

all failed to get greater constrictor effects from the blood of patients having high pressure than with blood from normal persons. Kretschmer's[71] results with the Meyer method were positive in acute and negative in chronic nephritis. However, the extreme vasoconstriction produced by the defibrinated blood or serum which all used seemed to reproduce the effect of epinephrin so exactly that the presence of this in normal blood was accepted without question.

On the basis of Langley's and Elliott's studies of the relation of epinephrin to the sympathetic nervous system[72] it began to be assumed that the maintenance of normal vascular tonus in the intact animal and man must be altogether dependent upon the constant secretion of epinephrin into the blood by the chromaffin tissue in the medulla of the suprarenal and elsewhere. The more this was taken for granted, however, the more difficult did it become to understand why an epinephrin effect was so often absent in states of high blood pressure. In October, 1911, G. N. Stewart[73] published a severe criticism of all these experiments as based upon inadequate evidence that epinephrin was the substance causing the reactions described. He called attention to the fact, which most of the clinical investigators had disregarded, that the property of stimulating the smooth muscle of artery or pregnant uterus is not peculiar to epinephrin. He suggested that as epinephrin evokes from certain other smooth muscle preparations, the intestinal ring for instance, the opposite effect, inhibition with loss of tone, no test for it in complex body fluids should be considered positive which did not demonstrate both types of reaction in the sample examined.

The beautiful dream of adrenalinemia, however, was not seriously disturbed until O'Connor,[74] in March, 1912, published the results of his painstaking and ingenious investigation of the subject. He proved clearly that the vasoconstrictor substance in defibrinated blood and serum, which had been mistaken for epinephrin, was equally stimulating to intestinal peristalsis, and was therefore from this standpoint the antagonist of epinephrin. He furthermore proved that no constrictor effect was produced by blood which was prevented from coagulating by the addition of citrate or hirudin. The supposed epinephrin of defibrinated blood serum was apparently some substance produced during the process of clotting and not present in the circulating blood at all. Definite evidence of epinephrin in the blood he could obtain only in that from the adrenal veins.

[71] Ueber die Aetiologie der nephritischen Blutdrucksteigerung und vergleichende experimentelle Untersuchungen über blutdrucksteigernde Substanzen, Kong. f. inn. Med., 1910, xxvii, 731.

[72] Artur Biedl, Innere Sekretion, Berlin, 1910, p. 212.

[73] So-called Biological Tests for Adrenalin in Blood, with Some Observations on Arterial Hypertonus, Jour. Exper. Med., 1911, xiv, 377.

[74] Ueber den Adrenalingehalt des Blutes, Arch. f. exper. Path. u. Pharmakol., 1912, lxvii, 195.

The further researches of Stewart,[75] published very recently, while confirming the absence of epinephrin reactions in peripheral blood, go to show that the whole subject is complicated and that the mere prevention of clotting does not always suffice to make shed blood an indifferent fluid to smooth muscle. Bloods kept from clotting by citrate, hirudin, and peptone are not identical in their effects. These studies again emphasize the need for extreme caution in interpreting the biologic reactions obtained with so complex a fluid as blood as due to any one supposed constituent.

Before the publication of O'Connor's article, Park and the writer,[76] as the result of a long series of experiments made by a modified Meyer method, had already reached the conclusion that the vasoconstrictor substance of defibrinated blood was not epinephrin. We used as our test objects rings of the carotid artery of the ox which are constricted by epinephrin, and rings of the coronary which undergo dilatation.[77] Defibrinated blood and serum produced extreme constriction of both preparations. The character of the curve was different from that produced by epinephrin; it was similar to that of barium chloride, a substance known to act directly upon smooth muscle, whereas the point of attack of epinephrin is the so-called "receptive" substance, the neuromuscular junction between the sympathetic nerve fiber and the smooth muscle. It was clear that the serum constrictor substance acted upon smooth muscle directly and had no relation to its sympathetic innervation. We had made a number of unsuccessful attempts to identify low dilutions of epinephrin in serum. After the publication of O'Connor's work we studied normal human blood and blood from six patients having high pressure, with and without nephritis. In most of the experiments we prevented clotting of the blood by the use of hirudin, in a few by citrate. Neither in normal blood nor in the blood from hypertensive patients could any definite trace of an epinephrin effect be obtained.

O'Connor's results have also been amply confirmed by Schultz[78] who has, however, made no studies of nephritic blood. Using trustworthy methods, Cannon[79] and his collaborators, and Hoskins and McClure[80] have identified epinephrin in blood from the adrenal veins. Stewart[81] has only succeeded when the gland was disturbed or stimulated. He has failed to obtain any evidence of its existence in pathological sera.

[75] A Comparison of the Action of Plasma and Serum on Certain Objects Used in Biologic Tests for Epinephrin, Jour. Exper. Med., 1913, xvii, 152.

[76] Theodore C. Janeway and Edwards A. Park, The Question of Epinephrin in the Circulation and its Relation to Blood Pressure, Jour. Exper. Med., 1912, xvi, 541.

[77] Edwards A. Park, Observation with Regard to the Action of Epinephrin on the Coronary Artery, Jour. Exper. Med., 1912, xvi, 532.

[78] Physiological Studies in Anaphylaxis, Bull. Hyg. Lab., United States Public Health and Marine Hospital Service, 1912, No. 80.

[79] Emotional Stimulation of Adrenal Secretion, Amer. Jour. Physiol., 1911, xxviii, 64.

[80] The Adrenal Glands and Blood Pressure, Arch. Int. Med., 1912, x, 343.

Hoskins and McClure[82] feel confident that they have shown that the quantity of epinephrin necessary to produce a minimal rise in blood pressure is from ten to twenty times the amount secreted by the suprarenal glands per minute. As they have further shown that the injection of an amount sufficient to raise blood pressure causes a complete inhibition of intestinal peristalsis, they argue that adrenal secretion cannot be a direct factor in the maintenance of the normal tonus of the vasomotor system. They agree with O'Connor[83] in estimating the probable epinephrin concentration of general arterial and venous blood at 1 in 200,000,000, an amount undetectable by the most delicate methods.

The possible assumption remained that repeated doses of epinephrin below the minimum effective single dose might increase the tone of the vessels. Park has recently tested this for me on the artery strip. His results have been absolutely negative. Lieb has also performed a few experiments to try on the isolated vessel the supposed synergism of hypophysis extract and epinephrin, which Kepinow[84] claimed to find. He has been unable to confirm it.

The work of Cannon[85] and his collaborators, already alluded to, showed a marked increase in epinephrin output under the influence of anger, fear, and strong sensory stimulation. The splanchnic nerve seems to contain secretory fibers for the adrenal. Two articles by von Anrep[86] (from Starling's laboratory), which have just appeared, show that the normal effect of splanchnic stimulation in an intact animal is a short, primary rise in blood pressure, followed by a secondary rise, which is accompanied by increased tonus of the heart and marked peripheral vasoconstriction. Similar stimulation, after exclusion of the suprarenals by clamping the vein, results only in a moderate rise in pressure, continuous with the primary rise, with dilatation—not constriction—of the heart and the peripheral arteries. The conclusion drawn seems warranted—that the secondary effects of splanchnic stimulation are dependent upon the discharge of epinephrin into the blood stream.

Blood Sugar. The problem has been approached from one other side—namely, by the investigation of the blood sugar. It is well known that the injection of epinephrin into an animal whose liver contains glycogen, results in an increase of sugar in the blood, which if it reaches a sufficiently high percentage, produces transient glycosuria. It has therefore been reasoned that if hypertension be

[81] The Alleged Existence of Adrenalin (Epinephrin) in Pathological Sera, Jour. Exper. Med., 1912, xv, 547.

[82] The Adrenal Glands and Blood Pressure, Arch. Int. Med., 1912, x, 343.

[83] Ueber den Adrenalingehalt des Blutes, Arch. f. exper. Path. u. Pharmakol., 1912, lxvii, 193.

[84] Ueber den Synergismus von Hypophysisextrakt und Adrenalin, Arch. f. exper. Path. u. Pharmakol., 1912, lxvii, 247.

[85] Emotional Stimulation of Adrenal Secretion, Amer. Jour. Physiol., 1911, xxviii, 64.

[86] On the Part Played by the Suprarenal in the Normal Vascular Reactions of the Body, Jour. Physiol., 1912, xlv, 307. On Local Vascular Reactions and Their Interpretation, Jour. Physiol., 1912, xlv, 318.

associated with increased circulating epinephrin, hyperglycemia should be found. Patients with high blood pressure, with and without nephritis, have therefore been investigated by various observers, with conflicting results.[87] At present the problem is being investigated in my service at the Presbyterian Hospital by Geyelin. The following table illustrates the most striking hyperglycemia yet observed in chronic nephritis:

HYPERGLYCEMIA IN CHRONIC NEPHRITIS.

Date.	Diet.	Blood sugar per cent.	Urea per cent.	Blood pressure.
Nov. 25	Soft, NaCl poor	0.099	0.168	234 mm.
Dec. 20	Soft, NaCl poor	0.133	0.188	220 mm.
Jan. 18*	Glucose 100 grams. Two hours after glucose excreted in urine, 0.26 gram	0.201	..	230 mm.
Jan. 22*	Glucose, 100 grams. Two hours after glucose excreted in urine, 0.12 gram	0.192	..	225 mm.
Feb. 8*	N. poor, thirty-six hours after uremic convulsion .	0.1605	0.375	205 mm.

* Epinephrin tests made on samples taken on these days.

It will be noticed that the blood sugar has increased from a figure at the upper limit of normal to a marked hyperglycemia in eleven weeks, while the blood pressure was highest at the first and lowest at the last observation. This increase, while unrelated to the height of the blood pressure, has, however, been coincident with the advance of the kidney lesion, increasing uremic symptoms, and a rise in the urea content of the blood, indicating coincident nitrogen retention. These figures seem to me much more in accord with the theory of renal retention than of epinephrin hyperglycemia, though one cannot interpret them with any positiveness. In view of the possibility of technical errors and of retention of sugar by the diseased kidney, it is the part of wisdom to reserve opinion upon the whole question until extensive work has been done by the newer, accurate methods. Even should hyperglycemia prove to be frequent in such patients, it would be absurd to consider it more than suggestive of increased circulating epinephrin, as it might be dependent upon other wholly unrelated disturbances or renal impermeability.

[87] Neubauer (Ueber Hyperglykämie bei Hochdrucknephritis und die Beziehungen zwischen Glykämie und Glucosurie beim Diabetes mellitus, Biochem. Zeitschr., 1910, xxv, 284; Nephritis und Blutzucker, Arch. f. exper. Path. u. Pharmakol., 1912, lxvii, 192 to 193), especially, claims to have found marked increases in blood sugar; Hagelberg (Hypertension und Blutzucker, Berlin. klin. Woch., 1912, xl, 1877), Wieland (Oekonomie des Blutzuckers, Zentralbl. f. d. gesamm. Physiol. u. Path. d. Stoffwechs., 1910, v, 481), and Port (Hypertension und Blutzucker, Deutsch. med. Woch., 1913, xxxix, 69) found significant increases only in cases with marked uremic symptoms, eclampsia, or apoplexy; Stilling (Nephritis und Blutzucker, Arch. f. exper. Path. u. Pharmakol., 1911, lxvi, 238), Tachau (Eine neue Methode der Bestimmung des Blutzuckergehaltes, Deutsch. Arch. f. klin. Med., 1911, cii, 597), Schirokauer (Zur Methodik der Blutzuckerbestimmung, Berlin. klin. Woch., 1912, xxxviii, 1783), and Frank (Bestehen Beziehungen zwischen chromaffinem System und der chronischen Hypertonie des Menschen, Deutsch. Arch. f. klin. Med., 1911, ciii, 397) have failed to find definite hyperglycemia. The latter worked especially with so-called essential hypertension cases.

In addition to this investigation, Lieb and I have recently made one more attempt to identify epinephrin in the peripheral blood from a patient in whom positive results might certainly be expected, if the epinephrin theory of hypertension has any basis. The patient was the one in whom the notable hyperglycemia was found (see page 641). The blood, prevented from clotting by hirudin, was tested on January 18 and 22 and February 8, on the last date thirty-six hours after a uremic convulsion; bleeding was done for therapeutic purposes. On the first date dilatation of the coronary was obtained, but of an extent comparable to that produced by not less than 1 to 10,000,000 epinephrin. At the same time a constriction of the peripheral artery was produced, but the form of the curve was different from any which I have ever seen due to epinephrin. This blood was also tested for its effect in dilating the pupil of the rabbit's eye, after removal of the left superior cervical ganglion. Meltzer[88] has found this an extraordinarily delicate test for epinephrin. A slight increase in diameter was observed in two such eyes, the control eye and the eyes of control rabbits showing no dilatation, or slight constriction. The light conditions for this test were, however, not entirely satisfactory.

For this reason additional tests were made on January 22. In these the carotid response was typical of epinephrin; the coronary, however, showed a primary constriction, followed after three minutes by a marked dilatation. This cannot be claimed as an epinephrin response, though it is possible that it may be the combination of an epinephrin effect with vasoconstriction from some other substance in the blood. The rabbit intestine test with the same blood was only faintly suggestive, in no way corresponding to the effect which might have been expected from the constriction produced in the carotid. The final test on February 8 gave a satisfactory carotid response, but a constriction of the coronary, followed after a still longer interval than in any other case by dilatation and an inhibition of the intestine so extreme and protracted as to be impossible with any concentration of epinephrin which would not have given the most typical results with the two artery preparations. These findings while in many particulars highly suggestive of the presence of epinephrin, are entirely too variable to permit me to believe that we have identified it.[89]

[88] Studies on the "Paradoxical" Pupil Dilatation Caused by Adrenalin. I. The Effect of Subcutaneous Injections and Instillations of Adrenalin upon the Pupils of Rabbits, Amer. Jour. Phys., 1904, xi, 28.

[89] This patient died in uremic coma on February 17. Autopsy revealed an extreme degree of atherosclerotic contracted kidney, and adrenals which weighed 10.37 and 8.71 grams respectively—more than twofold the normal—with abundant medulla. Estimation of the epinephrin in half the left gland, by Folin's new method (Otto Folin, W. B. Cannon, and W. Denis, A New Calorimetric Method for the Determination of Epinephrin, Jour. Biol. Chem., 1913, xiii, 477) showed a content of 3.1 milligrams. The determination from the right adrenal was spoiled. The gland was cut so as to divide the medulla as equally as possible. On this basis the total epinephrin content of the two adrenals should have been 13.5 milligrams, three times Ingier and Schmorl's average figure. Histologic study of the remaining halves of the glands, while showing a large medulla, failed to show a striking increase in chromaffin substance.

In order to test still further the possibility of detecting epinephrin in the blood, Lieb and I have performed a final series of experiments on four dogs. These dogs were anesthetized and samples of blood were drawn from the right femoral artery, one into hirudin and one into citrate solution. Then a continuous infusion of epinephrin in normal saline, according to Kretschmer's method,[90] was introduced into the right femoral vein. This produced a sudden and extreme hypertension, 200 mm. or over, for at least ten minutes in the shortest experiment. Blood was taken from the left femoral artery at the end of the infusion, while the blood pressure was still high, and its action on carotid and coronary strips and the intestinal segment compared with that of blood drawn before the production of epinephrin hypertension. The results of these four experiments are very disappointing. While in all we obtained positive tests with one or two of the test objects used, in no single experiment did we succeed in producing unequivocal epinephrin reactions in all three test objects. As shown by Stewart,[91] foreign blood has at times very disturbing effects upon these living smooth muscle preparations.

The amount of epinephrin injected into three dogs was 0.05 mg., and for one 0.1 mg. per kilo. Figuring the blood volume of the dog at the minimum of 5 per cent., this would make the concentration of epinephrin, if the blood and epinephrin had been mixed outside the body, 1 in 1,000,000. In our last experiment the intestinal segment showed a mere suggestion of a response, whereas a perfectly distinct effect was produced by blood containing added epinephrin in concentration of 1 to 25,000,000. Such an experiment shows the extreme rapidity of disappearance of epinephrin from the circulation. The immediate fall of pressure at the end of the infusion also suggests prompt destruction or fixation of the substance, though explicable as well by Straub's[92] theory of toxic action, as illustrated by muscarin.

From these experiments I am persuaded that the attempt, by our present methods, to obtain evidences of epinephrin in the peripheral circulation is fruitless. I should go farther than Stewart[93] and insist that no demonstration be considered conclusive which did not show qualitatively typical and quantitatively possible epinephrin effects, simultaneously in three different test objects, inasmuch as many confusingly similar effects may be produced by substances contained in that highly complex fluid, blood. To

[90] Dauernde Blutdrucksteigerung durch Adrenalin und über den Wirkungsmechanismus des Adrenalins, Arch. f. exper. Path. u. Pharmakol., 1907, lvii, 423.

[91] A Comparison of the Action of Plasma and Serum on Certain Objects Used in Biologic Tests for Epinephrin, Jour. Exper. Med., 1913, xvii, 152.

[92] Zur chemischen Kinetik der Muskarinwirkung und des Antagonismus Muskarin-Atropin, Pflüger's Arch., 1907, cxix, 127.

[93] So-called Biologic Tests for Adrenalin in Blood, with Some Observations on Arterial Hypertonus, Jour. Exper. Med., 1911, xiv, 377.

obtain these three reactions, as we have shown, even when epinephrin is known to be the cause of the very high blood pressure, is a matter of great technical difficulty with the biologic test objects at present employed.

To recapitulate, the net result of all this labor is the solid, well-grounded fact that the suprarenal glands, or at least their medullary portions, manufacture a substance, epinephrin, which introduced into the circulating blood produces a rise in the systemic arterial pressure unparalleled in intensity by any other known substance. This rise is extremely transient; but the continuous, steady introduction of epinephrin is capable of maintaining a state of hypertonus as long as the introduction is continued. Accompanying this rise in blood pressure is a reduction in volume of the extremities and of many organs, due to local vasoconstriction, so that the actual blood flow through them is diminished. The coronary artery, however, is dilated by epinephrin, and intestinal peristalsis is inhibited and intestinal tonus abolished. The bronchi in a state of spasm are also relaxed by epinephrin. It is probable that during life epinephrin is constantly finding its way from the adrenals into the general circulation, but except in the blood of the adrenal veins, epinephrin has never been positively identified in the general circulation of the normal animal or man. From all the quantitative studies that have been made, as well as from other considerations, it cannot at present be assumed that epinephrin exists in the general circulation in sufficient concentration to manifest any of its physiologic actions; but during stimulation of the splanchnic nerve, either directly, reflexly, or psychically, the rate of epinephrin discharge into the circulation may be markedly increased and its action become evident. This, as Hoskins and McClure[94] suggest, should probably be regarded as a reserve mechanism of the organism to meet emergencies. Up to the present time epinephrin has not been proved to play any part in the maintenance of normal vascular tonus. There is no convincing evidence, anatomic or physiologic, for any theory connecting the adrenal glands or increased circulating epinephrin with states of high blood pressure, with or without nephritis. That for some types of hypertension, or for certain acute and transient crises of hypertension, increased epinephrin discharge may in the future be demonstrated as the cause can be neither affirmed nor denied.

II. Clinical Facts. From the contentious realm of theory and experiment I ask you to return to the more peaceful, though perhaps prosaic, domain of clinical facts. Experimental medicine has not as yet solved the riddle of hypertension; there is need for further work in that field. Nor can clinical medicine make this claim; but the facts gained by the observation of human blood pressure

[94] The Adrenal Glands and Blood Pressure, Arch. Int. Med., 1912, x, 343.

in disease have added greatly to our knowledge of the pathology of the circulation. They are fundamental to an adequate understanding of the theoretic problems to be solved in the laboratory and the practical problems to be dealt with at the bedside.

What do we mean by high blood pressure? That question is more easily answered today than it was nine years ago, because the requirement of a blood pressure reading by many life insurance companies as a part of the examination of the applicant has made available the records of large series of normal individuals. From the compilations of Woley,[95] Fisher,[96] and Cook[97] it is clear, as I had held previously,[98] that a constant systolic blood pressure of 160 mm. or over is pathologic. It seems probable, as Cook suggests, that more extended observations will make 150 mm. the upper normal limit. Before middle life pressures of over 135 mm. are suspicious, above 145 mm. abnormal. In Woley's series, the average for women was 7.5 mm. lower. First readings in any person are apt to be higher than subsequent ones. When the use of the sphygmomanometer becomes as much a matter of daily routine as the taking of temperature, a still more accurate guide to pathologic variations in blood pressure will be afforded by comparing the previously recorded normal pressure of the person in question. I cannot too strongly urge on practitioners the need for keeping occasional records of the arterial pressure of all patients in order that early evidences of disease may be recognized and that our knowledge of the manner in which hypertension develops may be extended.

High blood pressure is a symptom so common that its chief manifestations are familiar to all physicians. General impressions, however, may mislead; and in order that I might present a basis of definite facts, I have made an analysis of the histories of 459 private patients whose systolic blood pressure registered over 165 mm. These records extend over a period of ten years. Upon this analysis and the survey of a selected group of hospital patients any opinions that I may express are founded.

From a study of this kind it is clear that the patients naturally fall into certain groups as regards symptoms and clinical course. The largest group is made up of individuals well past middle life. The clinical picture which they present is usually that of some degree of cardiac insufficiency, and their death is a cardiac death. Arteriosclerosis is a commonly associated lesion; anginoid attacks are fairly frequent; about 10 per cent. are elderly diabetics. While

[95] The Normal Variation of the Systolic Blood Pressure, Jour. Amer. Med. Assoc., 1910, lv, 121.

[96] The Diagnostic Value of the Use of the Sphygmomanometer in Examinations for Life Insurance. Meeting of Association of Life Insurance Medical Directors, October 4, 1911, New York.

[97] Blood Pressure in Prognosis, Medical Record, 1911, lxxx, 959.

[98] Theodore C. Janeway, Diagnostic Significance of High Arterial Pressure, Amer. Jour. Med. Sci., 1906, cxxxi, 772.

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[98] Theodore C. Janeway, Diagnostic Significance of High Arterial Pressure, Amer. Jour. Med. Sci., 1906, cxxxi, 772.

the bulk of them at some period show albumin, casts, or other urinary changes, usually interpreted as indicating nephritis, and while at autopsy the majority prove to have either arteriosclerotic atrophy of the kidneys or the so-called "primary contracted kidney," it must be borne in mind that during life many of these individuals fail to show any urinary changes other than those of chronic passive congestion. There are also a number of authenticated autopsy cases on record in which the same clinical picture of permanently high blood pressure has been associated with kidneys found to be normal or with only secondary congestion, due to a failing heart. I have seen such patients, and Krehl[99] and Schlayer[100] have published records of similar ones. When these individuals consult a physician because of even minor symptoms, the blood pressure is usually found already far above normal, and although some reduction and great symptomatic improvement may occur as the result of hygienic and dietetic measures, I have only a single unequivocal record of a patient in whom the pressure returned to the normal for as long as two years. In the main, the treatment of these patients lies in safeguarding the heart. From the clinical standpoint I speak of them as cases of hypertensive cardiovascular disease.

A closely related group shows predominant cerebral symptoms —headache, vertigo, apoplectic attacks. Polyuria is found more frequently in this group and the evidences of severe functional damage to the kidneys. Far more of them die with uremic symptoms. The discrimination between toxic cerebral symptoms and manifestations of focal vascular lesions, or of general cerebral arteriosclerosis, is so often impossible during life that this clinical group must be considered a compound one. On the one hand it contains the older individuals whose important disease is arteriosclerosis of the brain arteries; on the other, younger persons with the so-called primary contracted kidney. A quite similar clinical picture may occasionally be presented by chronic glomerular nephritis.

Many attempts have been made to correlate the clinical picture, the functional disturbance of the kidney as revealed by the newer tests, and its anatomic lesions found at autopsy. None of these has succeeded, and at present it seems a far cry to the day when such attempts will be successful. Schlayer[101] remarks with much reason that when we speak of chronic interstitial nephritis we usually have in mind a definite symptom-complex rather than an anatomic picture, and that much of the misunderstanding between

[99] Ueber die krankhafte Erhöhung des arteriellen Druckes, Deutsch. med. Woch., 1905, xxxi, 1872.

[100] Untersuchungen über die Funktion kranker Nieren, Deutsch. Arch. f. klin. Med., 1911, cii, 371.

[101] Neue klinische Anschauungen über Nephritis, Beihefte z. med. Klin., 1912, viii, 9, 211.

pathologists and clinicians has arisen from this fact. It seems to me that we should recognize clearly that the differentiation of the various anatomic types of nephritis is altogether beyond the powers of clinical diagnosis. Fortunately it is not of great import for us as internists, for we are practically concerned with structural changes only insofar as they give rise to disturbances of function, can be utilized for diagnosis, or afford us data for prognosis. Rarely, indeed, can we influence them directly. The kidney is a highly complex organ and the contribution of each of its structurally differentiated parts to its total function is unknown. If correlation of structure and function is thus still impossible to the physiologist, the physician need not be ashamed of his failure to harmonize them when diseased. For the present, in the clinical study of renal disease, the aim must be to achieve an exact analysis of the perverted functions and to discover the evidently remote causes, as a basis for treatment and prevention. I believe that the conception of hypertensive cardiovascular disease is justified on this physiologic basis.

When so obvious a disturbance of the circulation exists and investigation of the kidney function shows no changes of importance it is immaterial what may be the exact appearance of the kidney; the patient must be treated from the standpoint of the circulatory disorder. The more recent pathologic anatomic studies seem to justify this rather barefaced clinical point of view. In particular the work of Jores,[102] Aschoff,[103] and Gaskell[104] shows a return of pathologists to the fundamental idea which Gull and Sutton[105] enunciated—namely, that the real disease back of what we call chronic interstitial nephritis is a disease of the small blood-vessels and that the lesions of the kidney are secondary manifestations. Gull and Sutton may have been misled by inadequate histologic methods into an erroneous interpretation of the vascular lesion, but their arteriocapillary fibrosis stood for the conception of primary vascular disease. The return to the interpretation of the primary contracted kidney as essentially a disorder of the kidney arterioles has been facilitated by Löhlein's[106] differentiation of the secondary contracted kidney, which arises out of a true glomerular nephritis, from the former confused group of atrophic kidneys. While there may be an overlapping of types and various combinations of lesions within the same kidney, and while it is

[102] Ueber die Arteriosklerose der kleinen Organarterien und ihre Beziehungen zur Nephritis, Virchow's Arch., 1904, clxxviii, 367.

[103] Kritisches zur Lehre von der Nephritis und den Nephropathien, Med. Klinik, 1913, ix, 18.

[104] On the Changes in Glomeruli and Arteries in Inflammatory and Arteriosclerotic Kidney Disease, Jour. Path. and Bact., 1912, xvi, 287.

[105] On the Pathology of the Morbid State Commonly Called Chronic Bright's Disease with Contracted Kidney, Med.-Chi. Trans., 1872, lv, 273.

[106] Ueber Nephritis nach dem heutigen Stande der pathologisch-anatomischen Forschung, Ergebn. d. inn. Med. u. Kinderh., 1910, v, 411.

still beyond the possibilities to agree upon either the clinical symptoms or the functional disturbances which are associated with these different types—as such studies as those of Volhard[107] and Frey[108] show—there does seem to be sufficient anatomic basis for the belief that the hypertensive cardiovascular disease which we recognize clinically is not primarily nephritic hypertension (in the strict sense of the term) but widespread disease of the arterioles in various internal organs.[109] The disease in its fully developed form involves the kidney, producing the small, red, granular, or primary contracted kidney; but occasionally it leaves the kidney untouched. In its course arteriosclerosis of the larger vessels may develop, hypertrophy of the heart is frequent, and death by apoplexy a common mode. On the other hand arteriosclerosis of the larger vessels may spread peripherally, as it were, and become associated with a similar clinical picture, though less constantly leading to high blood pressure and a hypertrophied heart. This primary arteriosclerotic disease produces the patchy arteriosclerotic atrophy of the kidney rather than the more diffuse changes of the arteriolar disease. Clinically this form is perhaps more commonly associated with an insufficient heart. From the standpoint of physiology the high blood pressure is the evidence of arteriolar disease rather than renal, though it is premature to consider the relation quantitative in any sense. It must be interpreted as a sign of abnormal irritability of the constrictor mechanism. Whether it precedes the development of the anatomic lesions, as Allbutt[110] and the English school have held, as Huchard[111] meant by his term "pre-sclerosis," as von Basch[112] taught in his conception of "angiosclerosis," and as Jores[113] seems to believe, cannot be regarded as settled. That it is, however, primarily dependent upon processes without the kidney seems altogether probable.

Have we any clue to the origin of this persistent vascular spasm? We have seen that the epinephrin theory is without verification. Were it proved it would only explain the mechanism, not its cause, and carry the problem one step farther back. Many experienced clinicians have believed that high blood pressure is in some way related to overindulgence in food, the abuse of tobacco, of coffee, and other poisons, and the sedentary life, which characterize the well-to-do in our western civilization. Allbutt's hyperpiesis expresses this view. The results of treatment sometimes lend strong support

[107] Ueber die funktionelle Unterscheidung der Schrumpfnieren, Kongr. f. inn. Med., 1910, xxvii, 735.

[108] Zur Pathologie der chronischen Nephritiden, Deutsch. Arch. f. klin. Med., 1912, cvi, 347.

[109] Kritisches zur Lehre von der Nephritis und den Nephropathien, Med. Klinik, 1913, ix, 18.

[110] Arteriosclerosis and the Kidneys, British Medical Journal, April 15 and 22, 1911 i, 853, 992.

[111] Traité cliniques des maladies du cœur et des vaisseaux, Paris, 1893.

[112] Die Herzkrankheiten bei Arteriosklerose, Berlin, 1901.

[113] Ueber die Beziehungen der Schrumpfnieren zur Herzhypertrophie vom pathologisch-anatomischen Standpunkt, Verhandl. deutsch. path. Gesellsch., 1908, xii, 187 (see editorial, Jour. Amer. Med. Assoc., 1909, lii, 565); Deutsch. Arch. f. klin. Med., 1908, xciv, 1.

to it. In a recent case, for instance, a gentleman of sixty-two years, who showed at the subsequent autopsy an early stage of vascular kidney disease, underwent a Tufnell cure for thoracic aneurysm. The systolic pressure fell from 220 to 125 mm., after a hemorrhage once reached 70 mm., and yet returned to 190 mm. before death. Remarkable drops are seen in hospital patients after rest in bed with salt-poor diet, but the pressure usually rises moderately as soon as activity is resumed. Such reports as that of Hecht[114] show how much the tension may be modified during sanatorium treatment, in which muscular training, massage, bland diet, limitation of fluid and of salt, and abstinence from tobacco, spices, and coffee coöperate with freedom from home and business cares to reduce the activity of the constrictor mechanisms. How much of this is central, how much peripheral, and which of the many changes in external conditions and internal relations is preponderant in accomplishing the result is not clear. But, again, some persons of abstemious life develop hypertension, and in most of these, treatment effects no marked or permanent change in the blood pressure.

A conspicuous feature in many of these patients is the variability of the pressure, especially the systolic pressure, within short periods, often from hour to hour (Hensen,[115] Israel[116]). All the causes of slight elevation of pressure in the normal person produce exaggerated effects in them. Vasodilators also, such as the nitrites, usually evoke a prompt though temporary response. Only in rare cases do the vessels cease to react. My experience is in entire accord with Matthew,[117] Miller,[118] and Wallace and Ringer[119] in this respect. Intercurrent acute disease usually produces a marked fall. These facts show clearly, I think, that disturbed vasomotor regulation, not permanent vascular obliteration, is the usual important factor. Volhard[120] makes the interesting observation that this type of disease is rare in Japan, and future statistics of vegetarian races may help to fix responsibility.

Gout and hypertensive nephritis are usually associated, and the clearing up of the causation of gout will illuminate our problem. One poison, however, which in rare cases produces acute gout, is

[114] Ueber die diatetische Beeinflussung pathologischer Blutdrucksteigerungen, Zeitschr. f. klin. Med., 1912, lxxvi, 87.

[115] Beiträge zur Physiologie und Pathologie des Blutdrucks, Deutsch. Arch. f. klin. Med., 1900, lxvii, 438.

[116] Klinische Beobachtungen über das Symptom der Hypertension, Samml. klin. Vorträge, Nos. 449 and 450 (Serie xv, 29–30), Inn. Med., No. 135–136, 1907, p. 853.

[117] Vasodilators in High Blood Pressure, Quart. Jour. Med., 1909, ii, 261.

[118] Hypertension and the Value of the Various Methods for its Reduction, Jour. Amer. Med. Assoc., 1910, liv, 1666.

[119] The Lowering of Blood Pressure by the Nitrite Group, Jour. Amer. Med. Assoc., 1909, liii, 1629 and 1630.

[120] Ueber die funktionelle Unterscheidung der Schrumpfnieren, Kongr. f. inn. Med., 1910, xxvii, 735.

the single cause of hypertensive cardiovascular disease upon which we can definitely put our fingers. That poison is lead. Vaquez[121] and Pal[122] have shown that lead colic is as truly a vascular crisis with transient hypertension as it is an intestinal cramp with constipation. As acute lead poisoning is thus a cause of marked acute vascular hypertonus, and chronic lead poisoning is known to be prolific of permanent hypertension, arteriosclerosis, and contracted kidney, one is strongly tempted to believe that the eventual anatomic vascular lesions are the sequel of the persistent vascular overstimulation. The suggestion then arises that other poisons as yet unknown act in a similar manner upon the bloodvessels. To carry the train of thought farther is unprofitable, and such poisons must be isolated and their actions demonstrated before such a theory can be useful. That in most cases of high blood pressure they are not retention products in the ordinary sense is clear, as gross retention does not exist in these patients until late.

The theory of intoxication by substances held back by the damaged kidney cannot be entirely discarded, however. The observation of cases with partial or intermittent ureter obstruction taught Cohnheim[123] long ago that hypertrophy of the heart and high arterial pressure might result. I have seen excision of the only functionating kidney lead to a rise in blood pressure four days after to 180 mm.; it fell again toward death. Pässler[124] and Brasch,[125] report interesting cases of long-standing anuria, due to bilateral ureter compression by pelvic carcinoma in women, with marked hypertension. One case of Brasch's rose from 115 to 210 mm. after three days of anuria. In these instances neither edema nor true uremia occurs, but acute hypertension is the rule. They seem quite analogous to the results of experimental quantitative reduction of kidney substance. Whether this is due to normal metabolites or abnormal compounds is not clear. Pearce's[126] interesting observations on the depressor substance of dogs' urine suggest the possibility that a normal balance between pressor and depressor substances in the blood may be maintained by the kidney.

I believe that the rise in blood pressure which may accompany anuria in such toxic necroses of the kidney as are produced by bichloride of mercury, for instance, belongs in the same category.

[121] La tension arterielle dans le saturnisme aigu et chronique, Sémaine Médicale, 1904, xxiv, 385.

[122] Gefässkrisen, Leipsic, 1905.

[123] Vorlesungen über allgemeine Pathologie, Berlin, 1880, ii, 397.

[124] Beitrag zur Pathologie der Nierenkrankheiten, nach klinischer Beobachtungen bei totaler Harnsperre, Deutsch. Arch. f. klin. Med., 1906, lxxxvii, 569.

[125] Ueber die klinischen Erscheinungen bei langandauernder Anurie, Deutsch. Arch. f. klin. Med., 1911, ciii, 488–504.

[126] Concerning the Depressor Substance of Dog's Urine and its Disappearance in Certain Forms of Experimental Acute Nephritis, Jour. Exper. Med., 1910, xii, 2, 128.

Krehl[127] says this does not occur, but I have seen the pressure rise from 130 mm. on the first to 168 mm. on the fifth day of bichloride poisoning, remaining about 170 mm. until the ninth day and then fall until death on the thirteenth day. Friedrich Müller[128] reports a similar finding.

I believe it is also probable, from some conspicuous instances of improvement following prostatectomy, that the effect of long-standing obstruction of the urethra may be the superposition of a blood pressure rise of this type on an already existing hypertension. A few other cases that I have seen possibly fall into this category of quantitative renal insufficiency. I have in mind a patient with a blood pressure of 200, who at autopsy showed complete infarction of one kidney, and only chronic passive congestion of the other. A second patient had a rudimentary kidney on one side, with moderate, diffuse nephritis of the other; he died with explosive uremic symptoms. I have also seen cases of gradual destruction of the kidney by bilateral pyonephrosis, with hypertension and terminal uremia. In the later stages of decompensated valvular disease it is the rule to find the blood pressure above the normal, sometimes considerably so; and the sulphonephthalein test gives evidence of a marked impairment of kidney function. Such patients frequently die with cerebral symptoms, much like those seen in uremia. From the functional as contrasted with the anatomic standpoint it seems that chronic passive congestion may produce serious disturbances in the kidney, and that the hypertension seen in such cases may be dependent upon this factor.

It is well known that patients with congenital cystic kidneys in the end develop the clinical picture of contracted kidney, with hypertrophied heart, high pressure, and low gravity urine. I have seen a striking example of this kind. One is tempted to think of the terminal state as one of quantitative reduction of kidney substance to the danger point, and in so doing to strengthen the argument for a more definite relation between kidney function and hypertension than the consideration of the atherosclerotic group seems to warrant.

The rare cases of amyloid disease must be considered for the moment an insoluble mystery. The kidneys are the seat of the most extensive vascular lesions, with practically every glomerulus infiltrated with the waxy substance. Polyuria may be present early, but in pure cases there is no hypertension, and in many there is actually an extreme, subnormal pressure. I have observed two autopsy cases in which the pressure ran from 65 to 90 mm. for weeks. A satisfactory theory of nephritic hypertension must afford an interpretation of such phenomena. Were I convinced

[127] Pathologische Physiologie, 1912, Leipsic, 35.

[128] Ch. Thorel, Pathologie der Kreislaufsorgane, Ergebn. d. allg. Pathol. u. pathol. Anat., 1910, xiv, II, 133, quotes Friedrich Müller.

of the universal applicability of the epinephrin theory, I should believe that the extensive infiltration of the adrenals with amyloid, which is the rule when the other viscera are waxy, was a ready-made explanation. One cannot deny that this suggestion has a certain plausibility on its face; I offer it as it has occurred to me, without caring to infer much from it either way, until we have more positive evidence as to the relation of the adrenals to normal vascular tonus. I do not consider that the cachexia of these patients is adequate to account for their low blood pressure, though it may be one factor. From the functional standpoint it is important to note that the type of disturbance manifested by the amyloid kidney is usually that of obstinate edema, with marked salt retention. Now of the types of true chronic glomerulotubular nephritis least often associated with any change in the heart or blood pressure, the dropsical form stands out preëminently, and *vice versa*, hypertension is most extreme in those nephritics who exhibit no edema.[129] We are as yet too ignorant of the relations of the various excretory functions of the kidney, one to another, to base any theory upon such relations. Widal's[130] classification of the nephritides into albuminuric, hypertensive hydropigenous, and nitrogen retention types, while suggestive in its broad outlines, does scant justice to the infinite variety of nature. Such studies, however, as he has conducted with regard to functional disturbances in the kidney, and especially such accurate analyses of disturbance in the excretion of individual substances as Schlayer[131] and his coworkers have carried on, point the road toward our goal.

Observations of the blood pressure in true acute nephritis, a condition which even pathologists agree is entitled to its name, are scanty. Many observers have failed to find definite hypertension, but one can never be certain how marked the nephritis was. Certainly a moderate, though very definite, rise in blood pressure has in my experience accompanied severe acute nephritis in the few patients that I have been able to observe carefully. A particularly instructive case showed a rise to 165 mm. during the first week in bed, with a rapid fall as diuresis was established. He recovered completely, and my subsequent observations for almost six years have shown a constant pressure of between 115 and 125 mm. Recently a boy in the hospital who had acute nephritis following severe tonsillitis came in with a pressure of 190. He had slight general edema, and a sulphonephthalein output of 54 per cent. In five days his pressure had fallen to 100, the edema had

[129] A recent case, however, has shown practically complete absence of sulphonephthalein excretion; so the functional impairment was evidently profound.

[130] Les grands syndromes du mal de Bright, Jour. med. français, January 15, 1911.

[131] Untersuchungen über die Funktion kranker Nieren, Deutsch. Arch. f. klin. Med., 1909, xcviii, 17; Untersuchungen über die Funktion kranker Nieren beim Menschen, Deutsch. Arch. f. klin. Med., 1910, ci, 333; Untersuchungen über die Funktion kranker Nieren, Chronische vaskuläre Nephritiden, Deutsch. Arch. f. klin. Med., 1911, cii, 311.

disappeared, and the phthalein output had risen to 62 per cent. Rolleston[132] has recently reported a transient rise in blood pressure in twelve out of thirty-three cases of scarlatinal nephritis, mostly mild; the highest pressure reached was 150. Kurt Weigert[133] saw a pressure of 240 mm. in severe post-scarlatinal nephritis fall to 170 mm. before death. One of the most striking observations was that of Buttermann,[134] who observed a rise of 50 mm. within twenty-four hours from the onset of an acute scarlatinal nephritis. This is analogous to the stormy onset with initial uremic convulsions that one observes occasionally.

The subacute and chronic types of glomerulonephritis which, from Löhlein's[135] studies especially, we may feel justified in grouping with the acute inflammations of the kidney are somewhat variable in their effects on blood pressure. I have seen subacute nephritis, with obstinate edema and anemia and a practically constant blood pressure, scarcely ever above the normal. In the chronic cases, with terminal uremic symptoms, the pressure often runs high, though just before death it may show an extreme fall; in one case that I observed the fall was from 240 to 100 mm. during the last twenty-four hours of life. A number of these patients show marked atrophy of the kidney and belong in the group of secondary contracted kidney. Until recently they have not been differentiated from the general group of contracted kidneys. In practically all postmortem statistics they tend greatly to increase the proportion of cases with small kidneys in which marked cardiac hypertrophy has been lacking. Such individuals frequently have dilated and hypertrophied hearts and general dropsy in addition to the uremic symptoms. Roth[136] has described some of these patients with normal or scarcely increased blood pressure and no changes in the small or large bloodvessels. As a rule the blood pressure rises progressively as serious uremic symptoms supervene.

Uremic hypertension, a hypertensive crisis accompanying the more acute cerebral manifestations, amaurosis, etc., to which Pal[137] has devoted so much attention, is an undoubted clinical fact. It is in every respect similar to the behavior of the blood pressure in puerperal eclampsia (Vaquez,[138] Vogeler[139]). Lead poisoning

[132] Blood Pressure in Scarlet Fever, British Journal Children's Diseases, 1912, ix, 444; Jour. Amer. Med. Assoc., 1912, lix, 1829.

[133] Ueber das Verhalten des arteriellen Blutdrucks bei den akuten Infektionskrankheiten, Samml. klin. Vorträge, 1907, No. 459 (Serie xvi, 9), Inn. Med., No. 138, p. 64.

[134] Einige Beobachtungen über das Verhalten des Blutdrucks bei Kranken, Deutsch. Arch. f. klin. Med., 1902, lxxiv, 1.

[135] Ueber Nephritis nach dem heutigen Stande der pathologisch-anatomischen Forschung, Ergebn. d. inn. Med. u. Kinderh., 1910, v, 411.

[136] Ueber Schrumpfnieren ohne Arteriosklerose, Virchow's Arch. f. path. Anat., 1907, clxxxviii, 527.

[137] Gefässkrisen, Leipsic, 1905.

[138] Eclampsie puerperale et tension arterielle, Semaine Médicale, 1907, xxvii, 121.

[139] The Blood Pressure During Pregnancy and the Puerpurium, Amer. Jour. Obstet., 1907, lv, 490.

may also give rise to analogous symptoms. Briggs[140] has described hypertensive crises in arteriosclerotic subjects. It is such sudden and short-lived accessions of blood pressure that to me most strongly suggest increased activity of the adrenals. The search for epinephrin in the general circulation should be made especially during such periods. Free venesection is the ideal treatment; its effects are shown on the blood pressure chart as clearly as in the behavior of the patient.

Unfortunately I must pass with mere mention the frequent association of increased blood pressure with exophthalmic goitre and uterine fibroids; the development of permanent hypertensive disease in women after the menopause and in many elderly diabetics; the occurrence of symptoms of hyperthyroidism in chronic nephritis. All these are facts suggestive of a relationship between disturbances of the internal secretions and vascular hypertonus, though admitting of far more than one explanation. Perhaps it is well that the limitations of one lecture prevent excursions into this field.

III. Conclusions. To assemble all the facts, as I have tried to do, is surely one of the most melancholy things in the world as long as these facts remain unrelated. No one cares to look at a pile of bricks and stones, but as soon as these take their places in the structure for which they were shaped and assume those relations which were not seen so long as they remained mere building material, they take on real interest. The first step toward the construction of a scientific theory must always be the assembling of the materials, the next their scrutiny, to see how the parts may be fitted one to the other. The building of the theory comes last, and in the field under discussion must be left for the future. The facts I have outlined, however, impress me as falling logically into certain large groups. In conclusion I shall state my present views about them.

I cannot entirely agree with Krehl[141] that, in the main, nephritis as such has no influence on the circulation. To me, heart, arteries, and kidneys seem to stand in an intimate relationship one to the other; the influence of the kidney upon the circulatory system appears as unequivocal as the influence of the circulatory system upon the kidney. A disturbance in either may lead to results, which from the functional standpoint are indistinguishable, though the anatomic pictures be diverse. If the study of experimental nephritis has taught us anything it is this, that the degree and kind of impairment of kidney function can in nowise be inferred from the histologic changes discoverable in the kidney by our present methods.

The symptom of hypertension in renal disease can, I believe, arise in three ways:

[140] Certain Hypertensive Crises in Arteriosclerotic Subjects, Amer. Jour. Med. Sci., 1905, cxxx, 252.

[141] Pathologische Physiologie, Leipsic, 1912, 7th edition, p. 36.

1. Hypertension may arise through purely quantitative reduction of kidney substance below the factor of safety. It is difficult to conceive of this as other than a vascular hypertonus due to retained poisons of some kind. Its clinical paradigm is the hypertension accompanying bilateral ureter obstruction or the unfortunate surgical removal of the only functionating kidney. Possibly it is one factor which helps to produce hypertension in the contracted kidney.

2. Hypertension may arise in connection with the unknown intoxication which causes disturbances of the central nervous system and which we call uremia. This intoxication is not one of retention, in a strict sense, though it is most commonly present in those cases of advanced nephritis which manifest marked nitrogen retention. Clinically it is associated with severe acute nephritis, sometimes at its very onset, besides the subacute and chronic inflammatory affections of the kidney.

3. Hypertension may arise in primary irritability of the vasoconstricting mechanism from unknown, probably extrarenal causes, which lead eventually to arteriolar sclerosis. In this type the disease in the kidney is the sequence, not the cause, of the generalized vascular lesion. When it progresses to a condition of extreme atrophy, resulting in the true primary contracted kidney, a renal element may be added to the existing hypertension. In some cases arteriosclerosis of the larger vessels may spread peripherally and produce a similar form of disease. In these primary vascular diseases it is probable that eventual widespread narrowing of the arterial stream-bed in some cases produces a permanent organic increase in peripheral resistance.

What are the vascular poisons back of these types of hypertensive disease? That question no one can answer. That epinephrin may be one of them is possible; that it is the only one seems to me improbable. One may say the same for the secretion of the hypophysis. I believe it is likely that different poisons produce different types of hypertension. One toxic cause we can name with certainty, lead. Excessive stimulation of the central vasomotor mechanism must also play some part in producing the varied clinical picture.

The first and second types of hypertension may at any time be superimposed upon the third. While the second, the uremic type, must be considered dangerous in itself, hypertension in the arteriosclerotic or atherosclerotic kidney is best regarded as a compensatory effort of the organism, as Bier[142] first suggested, to be interfered with only when danger threatens, either of cardiac failure or of cerebral hemorrhage.

[142] Ueber die Ursachen der Herzhypertrophien bei Nierenkrankheiten, Münch. med. Woch., 1900, xlvii, 527.

In functional pathology, nephritis today presents the aspect of a threefold problem: the problem of edema, the problem of uremia, and the problem of hypertension. The first is well on the road to solution, and in practical therapeutics has lost most of its difficulties. Of the second we have barely scratched the surface. The third, seventy-five years after the first clear statement made by Bright, still baffles our best attempts at solution. That it will yield up its secrets through the increasing application of exact physiologic methods at the bedside and through the discovery of means for reproducing the lesions of chronic nephritis in animals, I confidently believe. Then, and not until then, may we hope for the final merging of morphology and physiology in a higher synthesis. The finished picture of nephritis will appear the same from either aspect; all specialization of function basing itself upon known differentiation of structure, and every alteration of structure manifesting itself by intelligible disturbance of function. It is the task of clinical medicine to effect this final reconciliation, for only the clinician must at all times look at disease from both points of view. In accuracy of observation and refinement of technique the medicine of that day may surpass ours by far more than our laboratories surpass the meagre equipment of Guy's of seventy-five years ago; but the method will still be the method of Richard Bright, the careful comparison of the symptoms studied during life with the lesions found after death.

THE CIRCULATION IN THE ARM OF MAN.[1]

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The circulation in an organ, though dependent primarily upon central conditions, such as the cardiac output and the pressure in the larger veins and arteries, is markedly influenced by the condition of the local bloodvessels. These mainly determine the local blood flow, they regulate the amount of blood held in the organ, and they modify the character of the local arterial pulsations. Few parts of the human body are sufficiently accessible for a study of the local circulation by satisfactory bloodless methods. To this rule, however, the extremities constitute an exception. The arm especially has long been an object of circulatory studies, and within recent years various refinements in older methods and the addition of several new methods have added materially to our

[1] Read at the Cleveland Academy of Medicine, November 15, 1912

knowledge of the circulation in this limb. While the accuracy of the methods available on man is not in general equal to the accuracy of the bloody methods employed on animals, nevertheless the results obtained on man are of peculiar interest. In the first place the radial pulse is so frequently examined by physicians that a broader scientific knowledge of the conditions which may affect this pulse is desirable. Again, the effect which psychic processes exert upon the circulation in a limb can be investigated far better in man than in animals. Finally, many pathological processes can be studied only as they occur naturally in man, and we must turn to patients therefore for a better understanding of these processes and of the effect of treatment upon them.

METHODS. The record of simple volume changes by means of the plethysmograph has been for years our most important method for studying local variations in the arm circulation. Although this method of study has contributed much to our knowledge even within the last few years, nevertheless plethysmograph records suffer from certain inherent defects. For example, they record changes in the arm volume without telling us anything about the circulation at the beginning of an experiment. Furthermore, changes in volume may be due to changes in the caliber of either arteries, capillaries, or veins, and constant and definite relations do not exist between such volume changes and the local blood flow.[2]

Veiel[3] has recently restudied the radial pulse. For this purpose he used the mirror recorders of O. Frank, which follow the details of the curves with great precision. Space will not permit a review of this work, but I will mention in passing that these and similar studies[4] have shown that the finer details of the radial pulse and even of the brachial pulse, differ greatly from those of the aortic and the carotid pulses. They are in fact peripheral pulses, and their form depends largely upon the condition of the local arteries. We[5] are now engaged in a study of the volume pulse of the arm and of the flow pulse in the brachial artery by means of the mirror recorders of Frank. The volume pulse of the arm, obtained from a plethysmograph, records the difference between the varying entrance of arterial blood and the constant or nearly constant exit of venous blood. If, for example, 2 c.c. of blood enters the plethysmograph by way of the artery with the primary pulse wave and at the same time $\frac{1}{4}$ c.c. leaves by way of the veins, then the swelling which is recorded as the volume pulse would amount to $1\frac{3}{4}$ c.c.

[2] V. E. Henderson, and O. Loewi, Ueber die Wirkung der Vasomotorenreizung, Arch. f. exp. Path. u. Pharm, 1905, liii, 56.

[3] Ueber die Bedeutung der Pulsform, Deut. Arch. f. klin. Med., 1912, cv, 249.

[4] O. Müller and E. Weiss, Ueber die Topographie, die Entstehung, und die Bedeutung des menschlichen Sphygmogrammes, Deut. Arch. f. klin. Med., 1912, cv, 320.

[5] A. W. Hewlett, J. G. Van Zwaluwenburg, and J. H. Agnew, Trans. Assoc. Amer. Phys., 1912.

If the veins are momentarily obstructed, or if the normal venous outflow is known, then the volume pulse becomes (or can be translated into) a record of the arterial inflow at each point of the pulse cycle. We shall speak of this as the flow pulse of the brachial artery, for most of the blood enters the portion of arm studied through this channel.

The tachograph of von Kries[6] attempts to record the variations in the velocity of the arterial blood stream to the arm, but it does not record the constant upon which these variations are superimposed.[7] Similar velocity curves may be derived by the method of Fick[8] from volume curves, and with present methods they should be more perfect technically.

Two methods for estimating the blood flow in the arm or hand of man have been recently described. The first of these, which we have mostly used is based upon a principle described by Brodie and Russell,[9] and will be spoken of as the plethysmographic method.[10] The patient lies in a reclining or semi-reclining position and the slightly elevated arm is placed in a plethysmograph, which is connected with a volume recorder. A narrow pressure cuff, similar to that used for determining blood pressure, is then placed about the arm, just outside of the plethysmograph. While the volume of the arm is being recorded the pressure in the cuff is suddenly raised to about the diastolic arterial pressure by opening a valve that places the cuff in communication with a large bottle containing air under pressure. The pressure in the cuff obstructs the veins, but leaves the arteries open. For a short time therefore the blood flows freely into the arm, but cannot escape. At this time the swelling of the arm, as indicated by the volume recorder, corresponds to the normal rate of arterial inflow. Naturally only the first portion of such a record can be used: (1) because the inflow is soon obstructed by the collection of blood in the veins and capillaries, and (2) because the rising venous pressure will eventually force blood beneath the obstructing cuff. The operation of these factors causes a gradual lessening in the rate of arm swelling, which is apparent on the tracings. The longer the period of a constant rate of swelling the greater the reliance that one may place on the accuracy of a given record. In order to increase the reservoir in which blood may collect without raising the pres-

[6] Studien zur Pulslehre, Freiburg, 1892.

[7] J. von Kries, Ueber die Methoden zur Beobachtung der arteriellen Blutströmung beim Menschen, Zeitschr. f. exp. Path. u. Therap., 1911, ix, 453; Christen, Tachogramm. Pulsvolumen. und Schlagvolumen, Zeitschr. f. exp. Path. u. Therap., 1911, ix, 607.

[8] Gesammelte Schriften, Würzburg, 1904, iii, 550.

[9] On the Determination of the Rate of Blood Flow Through an Organ, Jour. Phys., 1905, xxxii, p. xlvii.

[10] A. W. Hewlett and J. G. Van Zwaluwenburg, The Rate of Blood Flow in the Arm, Heart, 1909, i, 87. (The use of "we," etc., throughout this paper refers to work done by the author, either alone or in collaboration with other members of the staff in the Department of Internal Medicine, University of Michigan.)

sure in the vessels, a slight elevation of the arm, which tends to empty the veins, is of considerable technical importance.

The second method for determining the blood flow in the hand is that described by G. N. Stewart.[11] As it involves a measurement of the amount of heat given off from the hand in a calorimeter, it will be referred to as the calorimetric method. This method depends upon the principle that the heat thus given off is derived almost entirely from the blood that circulates through the hand. Knowing (1) the amount of heat given off from the hand, and (2) the temperature of the blood which enters and that which leaves the hand, one may calculate how much blood may have passed through in order to give off the heat eliminated.

Psychic Effects. Over thirty years ago, A. Mosso[12] showed that increased attention and mental work caused a diminution in the volume of the arm and in the size of the volume pulse. These observations have since been confirmed and extended by numerous investigators,[13] and the relation of these volume changes to those occurring in other parts of the body, as well as their relation to the different types of psychic stimuli, have been repeatedly studied. According to Weber the following changes in the distribution of blood in the body occur as a result of mental or emotional activity.

Weber's Table.

	Brain.	External head.	Abdominal organs.	Limbs and external trunk.
An impulse to motion with or without execution of the movement	+	−	−	+
Mental work	+	−	+	−
Terror (surprise)	+	−	+	−
Pleasure	+	+	−	+
Unpleasant sensations	−	−	+	−
Sleep	+	−	−	+

+ indicates an increase and − indicates a diminution in the content of blood in the part.

It will be seen that most emotional and mental processes, with the exception of pleasurable sensations, are associated with temporary decreases in the arm volume. These changes are accompanied by changes of a similar character in all the extremities and in the surface of the trunk and by changes of an opposite character in the volume of the abdominal organs—a reciprocal relation which is rather general, and is known as the Dastre-Morat Law. The above changes in arm volume are usually associated with corresponding changes in the size of the volume pulse.

[11] The Measurement of the Blood Flow in the Hands, Heart, 1911, iii, 33.

[12] Die Diagnostik des Pulses, Leipzig, 1879.

[13] A. Lehmann, Elemente der Psychodynamik, Leipzig, 1905. E. Weber, Der Einfluss psychischer Vorgänge auf den Körper, Berlin, 1910.

These psychic vasomotor changes also affect the blood flow through the arm. When the subject's attention or interest was aroused we have repeatedly observed a sudden reduction in blood flow, which might amount to 30 per cent. or more; and such sudden changes have occasionally proved confusing when the effect of other factors upon the blood flow in the arm was being studied. These sudden changes in blood flow are particularly marked in young and neurotic individuals.

Effect of Exercise. Since the experiments of Chauveau and Kaufmann[14] on the horse it has been known that the voluntary use of muscle is associated with a marked acceleration of the local blood flow, the increase in the experiments of these investigators being from four to nine times the resting flow. Volume changes in the arm of man during local exercise are difficult to measure by the plethysmograph, because the exercise disturbs the tracings; but direct measurements of the arm volume before and after exercise show increases in volume, which may amount to 200 c.c.[15] The rate of the blood flow in the arm of man is certainly markedly increased, for we[16] found the flow from three to eight times the normal immediately following local exercise, and Stewart obtained a definite increase for the hand in one experiment.[17]

Muscular contractions produced in animals by stimulation of the local nerves seem to be much less effective in accelerating the local blood flow.[18] Massage causes no arm swelling.[19] It would seem that the local circulatory changes are due only in small part to the mechanical effect of the muscular contractions; in the main they are due to vasomotor effects associated with the normal voluntary innervation of the muscles sent out from the higher nerve centres, for Weber[20] has shown that marked swelling of the arm may be induced in a motionless person during hypnotic sleep merely by the suggestion of motion in this arm.

Exercise of one arm has but little effect upon the blood flow in the other motionless arm. We have[21] found no change or a slight increase, and Stewart[22] found a moderate diminution. In Weber's experiments during hypnosis the volume of the opposite arm changed but slightly—sometimes in one direction and sometimes in the other. Vigorous exercise, with rise of blood pressure

[14] Compt. rend. de l'acad. des sciences, 1887, civ, 1126.

[15] Rancken, Ueber die Volumenverhältnisse des Armes bei Massage, aktiver Muskelarbeit und lokalem Heissluftbade, Skan. Arch. f. Physiol., 1910, xxiii, 55.

[16] A. W. Hewlett and J. G. Van Zwaluwenburg, loc. cit.

[17] G. N. Stewart, loc. cit.

[18] J. A. Tschuewsky, Ueber die Aenderung des Blutstroms im Muskel bei tetanischer Reizung seines Nerven, Arch. f. d. gesammt. Physiol., 1903, xcvii, 289; R. Burton-Opitz, Muscular Contraction and the Venous Blood Flow, Amer. Jour. Physiol., 1903, ix, 161.

[19] Rancken, loc. cit.

[20] Loc. cit.

[21] A. W. Hewlett and J. G. Van Zwaluwenburg, loc. cit.

[22] G. N. Stewart, loc. cit.

and warming of the body, will, however, increase the flow in an unused extremity. For example, immediately after violent exercise on the stationary bicycle the blood flow in the arm is considerably increased, but it falls with the fall of blood pressure, and the final level may be but little different from the original. In some individuals, however, the final level is somewhat raised due presumably to the warming effect of exercise.

THERMIC EFFECTS. The circulation in the arm is exceedingly sensitive to thermic influences, whether acting upon the local skin surface or upon some distant part of the body. When subjected to heat the arm becomes larger and softer, the skin becomes warm moist, and often reddened, the arteries feel large and soft, and the veins stand out prominently. All methods of study show that when heat is applied to the arm the bloodvessels tend to relax. The swelling of the arm may amount to 70 c.c.,[23] the volume pulse becomes larger,[24] the tachogram higher,[25] the blood flow may be increased from three to eight times the original,[26] and the venous pressure rises. If the application of heat causes pain there may be a temporary constriction of the vessels of the arm, owing to the psychic effect of the pain, following which the usual dilatation occurs. After the arm has been exposed for some time to high temperatures there is a tendency for the vessels to remain dilated and the blood flow rapid, even though the arm is subsequently somewhat cooled. It has been maintained, though to my mind not proven, that a paresis of the vessels exists in such cases.[27] Mild degrees of burn, as indicated by local reddening, which persists for days, are certainly due to a paralytic hyperemia, affecting chiefly the skin capillaries.

When the arm is exposed to local cold it tends to shrink. Gloves and rings fit more loosely, the skin feels cold and is pale or cyanotic, the radial artery is small and hard, the cutaneous veins become smaller or may disappear, the tachogram and volume pulse lessen in size, and the blood flow diminishes to one-fourth of the normal or even less. When the cold is intense and continued for some time the volume of the arm may again increase slightly,[28] and somewhat more heat is said to be given off from the hand at such extreme temperatures.[29] In most persons, however, we have been unable to obtain an increased blood flow during exposures to water sufficiently cold to cause considerable pain. The skin cyanosis and

[23] Rancken, loc. cit.

[24] A. Mosso, loc. cit.

[25] Balli, Ueber den Einfluss lokaler und allgemeiner Erwärmung und Abkühlung der Haut auf das menschliche Flammentachogramm, Dissertation, Bern, 1896.

[26] A. W. Hewlett, J. G. Van Zwaluwenburg, and M. Marshall, The Effect of Some Hydrotherapeutic Procedures upon the Blood Flow in the Arm, Arch. Int. Med., 1911, viii, 591.

[27] Ibid.

[28] U. Mosso, L'action du chaud et du froid sur les vaisseaux sanguins, Arch. ital de biol., 1889, xii, 346.

[29] Robinson and Stiles, External Temperature and Cutaneous Blood Flow, Amer. Phys. Ed. Rev., May, 1909.

swelling during exposure to cold can be explained as due to dilatation of the cutaneous capillaries and venules with edema without there being necessarily a dilatation of the smaller arterioles which chiefly govern the blood flow.

Changes in the room temperature markedly influence the blood flow in the arm. Variations of 50 per cent. in the flow may be produced by changes in room temperature[30] even when the subject feels subjectively comfortable. The variations produced by chilliness on the one hand to beginning perspiration on the other will cause variations in the flow through the arm that may amount to seven to ten times. The relation of these changes in the flow to the flow pulse of the brachial is interesting and instructive. Ordinarily most of the blood enters the arm through the brachial artery during the primary systolic pulse wave, and but little enters during the remaining portion of the pulse cycle. In a set of experiments on a normal individual[31] it was found that during exposure to a cold room the primary pulse wave was diminished about proportionally to the diminished flow, and that the main entrance of blood still occurred during the primary systolic wave. Approximately the same relation held during warming of the room up to moderately increased rates of blood flow. When the flow became very rapid, however, the size of the primary wave did not increase. At this time a continued rapid flow occurred throughout the entire pulse cycle. Apparently the large arteries had reached a maximum size, but the smaller arteries, which mainly govern the flow, had continued to dilate and allowed a rapid continuous stream to pass through them.

Thermic stimuli in addition to producing local changes in the circulation also influence the circulation in distant parts of the body. In general the application of heat or cold to one extremity causes a volume change in the same direction in the other extremities, and a volume change in the opposite direction in the abdominal organs.[32] Stewart[33] has shown that these vasomotor reflexes also affect the blood flow in the hand, and that they may be conveniently studied by plunging one hand in hot or cold water while the flow in the other is being recorded. The application of heat or cold to the interior of the stomach will cause a variation in volume of the extremities in the opposite direction from the effect of heat or cold applications to the skin (Müller[34]). Although the two arms tend to vary in the same direction it is possible when one

[30] A. W. Hewlett, The Effect of Room Temperature upon the Blood Flow, etc., Heart, 1911, ii, 230.

[31] A. W. Hewlett, J. G. Van Zwaluwenburg, and J. H. Agnew, loc. cit.

[32] O. Müller, Blutverteilung im menschl. Körper unter den Einfluss thermischer Reize, Deut. Arch. f. klin. Med., 1905, lxxxii, 547.

[33] The Effect of Reflex Vasomotor Excitation on the Blood Flow in the Hand, Heart, 1911, iii, 76.

[34] Loc. cit.

is exposed to cold and the other to heat for the flow to be slow in the former and fast in the latter.

It is evident, therefore, that thermic applications produce marked variations in the circulation in the arm, and that they may do this either through direct action or through distant reflexes. To what extent slight variations in the temperature of the blood may influence the peripheral blood flow through an action on the medullary centres has not been accurately determined for man. We know that in animals such action may occur,[35] and there is suggestive evidence that the temperature of the blood may be an important factor in the normal vasomotor control of man.[36] We have noticed repeatedly that when the body temperature has been somewhat reduced the blood flow through the arm tends to fall under slight provocation even though the local circulation had been fairly good previously.[37] Also, the general experience in hydrotherapeutic institutes has emphasized the importance of preventing heat losses sufficient to lower the body temperature when attempting to get a good reaction following cold procedures.

Other Physiological Factors. In addition to the effect of the psychic processes, exercise, and thermic influences it seems to us probable that other physiological factors may influence the blood flow in the arm of man, for in our experience the rate may vary considerably on different days even though the room temperatures are carefully controlled. As yet, however, we do not know the exact nature of these factors.

The Arm Circulation in Different Individuals. The blood flow in the arm varies considerably in different individuals. In our first paper[38] we stated that the flow usually lay between 2 c.c. and 4 c.c. of blood flow per 100 c.c. of arm substance per minute. A wider experience, however, has caused us to modify these figures. In our original experiments the subjects were usually stripped to the waist and the room was often somewhat chilly, both of which factors would tend to lessen the flows. At present we regard the usual variations of blood in the arms of normal individuals as from 2 c.c. to 8 c.c. of blood flow per 100 c.c. of arm substance per minute, while for a given individual variations of 50 per cent. are not uncommon. Stewart's figures for the hand varied from 3.5 c.c. to 14 c.c. of blood flow per 100 c.c. of hand substance per minute, while the variations in a given individual were insignificant. We have shown that this difference in rates as obtained by the two methods also holds on a single individual,[39] the caloric method

[35] Kahn, Ueber die Erwärmung des Carotidenblutes, Arch. f. Anat. u. Physiol. Physiol.; 1904, Abteil. Supplemental Band, p. 81.

[36] R. Stein, Zeischr. f. klin. Med., 1892, xx, 63.

[37] A. W. Hewlett, J. G. Van Zwaluwenburg, and M. Marshall, loc. cit.

[38] A. W. Hewlett and J. G. Van Zwaluwenburg, loc. cit.

[39] A. W. Hewlett and J. G. Van Zwaluwenburg, Comparison Between the Blood Flow in the Arm and in the Hand, Proc. Soc. Exp. Biol. and Med., 1911, viii, 111.

usually giving a more rapid blood flow in the hand relative to its volume than does the plethysmograph method for the arm, and we are inclined to attribute these differences to an actual difference in the circulation, the flow in the hand relative to its volume being greater than in the arm.

When we compare pathological individuals under ordinary conditions with these normal standards we usually find that their blood flows in the arm or hand fall within the normal limits of variation. This rule holds for such conditions as severe anemia, hypertension, and heart disease except in the stage of badly broken compensation. Slow rates are associated in general with cold extremities. The slowest that I have encountered was in a patient with dead fingers in whom the flow was 0.7 c.c. of blood flow per 100 c.c. of arm substance per minute. Stewart also found a slow flow in this condition. The most rapid flows are encountered in those with warm extremities, and of these patients with severe types of Graves' disease show the fastest rates. The most rapid rate that we have encountered under ordinary conditions of room temperature was 19 c.c. of blood flow per 100 c.c. of arm substance per minute.

During continuous fever the blood flow in the arm usually lies within the normal limits of variation. To what extent it differs from what would be the usual flow for the individual studied has not been determined. When the temperature is rising during fever the blood flow in the arm is relatively slow,[40] and during a chill the volume pulse becomes decidedly smaller.[41] When the temperature is falling, on the other hand, the flow is relatively fast and the volume pulse is large.

In general the size of the volume pulse in different individuals corresponds fairly well to the rate of blood flow in the arm, the larger the pulse the more rapid the flow, etc. The main entrance of blood into the brachial artery occurs during the primary systolic pulse wave, after which there is little or no flow. We have already pointed out that when an individual is very warm this relation does not hold, for the flow is then increased out of proportion to the increase in the primary wave and the blood enters the arm rapidly throughout all portions of the pulse cycle. This was found to be true also during muscular exercise and in the rapid flows of severe Graves' disease. In aortic insufficiency the opposite condition may hold. The volume pulse in typical cases is unusually large,[42] and following the primary wave an evident back flow throughout the remainder of the pulse cycle is sometimes but not always present. More blood, therefore, may enter the brachial artery during the primary wave than flows through the arm during the whole pulse cycle. This back flow in the brachial is not, however,

[40] A. W. Hewlett, loc. cit. [41] A. Mosso, loc. cit.
[42] A. W. Hewlett and J. G. Van Zwaluwenburg, unpublished observations.

characteristic of aortic insufficiency. As we shall see a short wave of backflow is evident in the nitroglycerin pulse, and probably occurs to a lesser extent under other circumstances. It seems possible also to have a slight continuous backflow in other conditions.

Vascular Reactions in Disease. The normal response of the vessels of the arm to psychic and thermic stimuli may be modified during disease. Two methods have been used for studying these abnormal vasomotor reactions. In the first, plethysmographic records are taken while the individual is subjected to some stimulus, such as mental work, pain, or the application of heat or cold to the skin. According to the second the blood flow is determined in one hand while the opposite hand is thrust into hot or cold water.

Weber[43] who has made a special study of psychic processes, found that there was a tendency for the usual vasomotor reflexes associated with attention, and the suggestion of movement to be lessened or even to be reversed during mental or physical fatigue. The reflexes normally produced by pleasant or unpleasant stimuli, on the other hand, were usually unaffected during fatigue. He states also that patients with Graves' disease, neurasthenia, or hysteria often showed such fatigue phenomena more readily than do normal individuals, and that in some of these patients this diminution or reversal of the normal reflexes was constantly present.

The vasoneuroses of which Raynaud's disease may be taken as a type have been studied by Curschmann, Simons, and Stewart. It is generally agreed that such patients usually show abnormal variations in their vasomotor reflexes. As yet, however, there is no general agreement as to character or constancy of these variations. Curschmann[44] found an abolition of the plethysmograph reactions to thermic and to various psychic stimuli. Simons[45] found variable reactions at different times and a lack of symmetry in the reaction on the two arms. Stewart[46] found a transient reaction to cold followed by an increase in the blood flow. It would seem not unlikely that such patients show considerable variations among themselves, and that a given individual may show different reactions at different times.

Organic lesions of the nerves or of the central nervous system may also affect the vasomotor reactions of the extremity. Simons[47] found that the vascular reactions of the hand depended upon an intact condition of the median and ulnar nerves and was inde-

[43] Loc. cit.

[44] Untersuchungen über das funktionelle Verhalten der Gefässen bei trophischen und vasomotorischen Neurosen, Münch. med. Woch., 1907, liv, 2519.

[45] Plethysmographische Untersuchungen der Gefässreflexe bei Nervenkranken, II, Arch. f. Anat. u. Physiol., Physiol-Abteil, 1910, Supplemental Band, 429.

[46] Loc. cit.

[47] Plethysmographische Untersuchungen der Gefässreflexe bei Nervenkranken, I, Arch. f. Anat. u. Physiol., Physiol-Abteil, 1910, 557.

pendent of the conditions of the radial nerve. Stewart found a transient reaction in patients with neuritis and an abolition of reactions in an old hemiplegic hand.

Arteriosclerosis, as shown by Romberg and his school[48] also tends to abolish the reflexes produced by the application of ice to the upper arm. It is interesting, however, that a thickened radial artery, especially in continuous hypertension, may show a normal or increased reaction. In such cases it may be assumed that the thickening is due to a hypertrophic muscle which shows normal or increased reactive power. In advanced heart disease the vascular reactions may be absent.[49]

THERAPEUTIC EFFECTS. Thus far we have accumulated relatively few data concerning the effect of drugs upon the circulation in the arm. It seems certain, however, that the most effective measures at our disposal for influencing this circulation are thermic stimuli applied either locally or to some distant part of the body. Skin irritants, such as mustard, produce a local dilatation of the cutaneous capillaries and venules, but their action upon the blood flow through the part, aside from thermic effects, is relatively slight.[50] One may reconcile these observations by assuming that the chief factor controlling the blood flow is the state of contraction of the small arterioles, and that mustard produces a dilatation of the cutaneous capillaries and venules without a corresponding dilatation of the underlying arterioles.

The intravenous injection of strophanthin[51] or digalen[52] in therapeutic doses affects neither the volume of the arm nor its normal reaction to the application of cold. Such injections are said, however, to affect the tonus of the larger arteries.[53] Intravenous injections of caffeine diminish the arm volume and intravenous injections of sodium nitrite increase it.[54] We have found that medicinal doses of nitroglycerin dropped on the tongue produce definite changes.[55] Within a few minutes the arm volume increases and the volume pulse becomes larger. The pulsations of the brachial artery as obtained by the Erlanger sphygmomanometer also become larger. The blood flow through the arm is not greatly affected. The flow pulse shows that a large arterial wave enters the arm and that

[48] Romberg and Müller, Ueber Bedeutung und Technik der plethysmographischen Funktionsprüfung gesunder und Kranker Arterien, Zeitschr. f. klin. Med., 1912, lxxv, 93.

[49] G. N. Stewart, loc. cit.; Romberg and Müller, loc. cit.

[50] C. I. Wood and P. G. Weisman, The Effect of a Skin Irritant on the Local Blood Flow in the Hand, Arch. Int. Med., 1912, x, 196.

[51] O. Vagt, Ueber die Herz und Gefässwirkung des Strophanthins bei gesundern und kranken Menschen, Med. Klinik, 1909, v, 1858.

[52] H. Eychmüller, Ueber die Herz und Gefässwirkung der Digalens bei gesunden und kranken Menschen, Berl. klin. Woch., 1909, xlvi, 1677.

[53] Nägele, Zentralbl. f. Herz. und Krankheiten, 1910.

[54] O. Müller, Ueber die Herz und Gefässwirkung einiger Digitaliskörper bei gesunden und kranken Menschen, Verhandl. des. Kongr. f. in. Med., 1909, xxvi, 364.

[55] A. W. Hewlett, J. G. Van Zwaluwenburg, and J. H. Agnew, loc. cit.

it is in large part immediately reflected. We have assumed in such cases a marked relaxation of the larger arteries of the arm, which allows a large pulse wave to enter, while at the same time the finer arterioles are contracted and do not allow the blood to flow through them. Owing in part to the relaxed condition of the large arteries the wave is reflected from the periphery.

Conclusions. In studying the local circulation in the arm of man, local conditions must be kept constantly in mind. The tachogram, the volume pulse, and the finer waves of the radial pulse depend in large part upon the condition of the larger arteries. The blood flow and the temperature of the part depend largely upon the condition of the finer arterioles. The color of the part depends in part upon the condition of the cutaneous capillaries and venules and in part upon the local flow. Changes in any of these cannot be referred unreservedly to changes in the heart action.

Many changes in the local circulation can be referred to thermic effects, and the function of the skin in serving as a physical means of heat regulation must be borne constantly in mind. Conditions of chilliness or warmth, whether occurring as a result of external temperature or as a result of fever, influence most markedly the peripheral circulation in the extremities. If we wish to increase the circulation in an extremity the most effective means at our disposal are general and local warmth. In comparison with these thermic measures the effect of drugs is insignificant.

AN INSTANCE OF PREMATURE BEATS ARISING IN THE AURICULOVENTRICULAR BUNDLE OF A YOUNG CHILD.

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AND

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E. H., a child, aged four and a half years, has been under observation for eighteen months or more, and whenever examined has shown premature beats of a curious but constant type.

Family History. Both parents are living and well. The mother has had at least one attack of rheumatism. Three sisters and brothers are living and well.

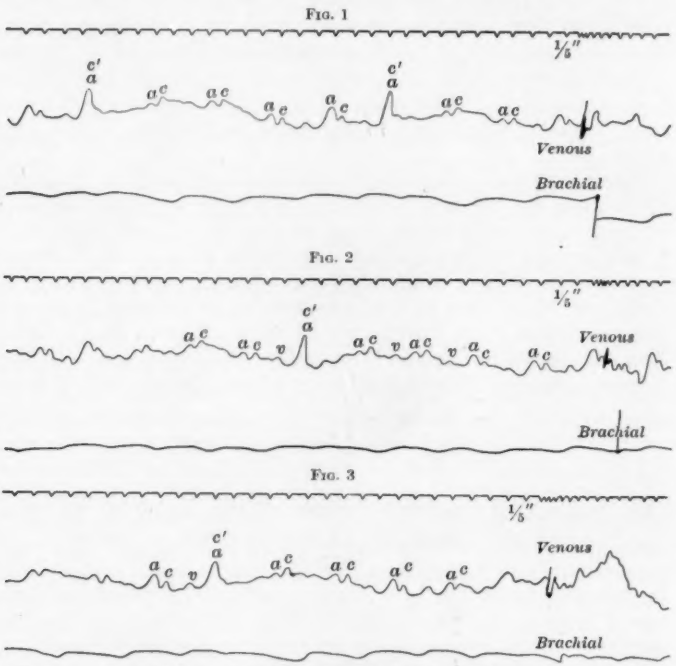
Previous Illness. As a baby had chickenpox. In November,

1910, had a severe attack of measles, lasting about four weeks. No history of rheumatic infection or other illness.

Examination shows a child somewhat small for his years, but apparently quite healthy. Is able to play and to get about without any evident cardiac distress.

Heart: Percussion outline normal. Sounds are everywhere clear. The normal rhythm is interrupted by moderately frequent premature contractions, each of which is accompanied by two heart sounds.

No abnormalities are detected in the other organs.



Figs. 1, 2, and 3.—Simultaneous tracings from the brachial and jugular pulses, each showing one or more premature beats.

Description of graphic records: In *polygraphic curves* (Figs. 1, 2, and 3) a slight degree of sinus arrhythmia is evident, and this rhythm is interrupted from time to time by premature beats, which, allowing for the sinus arrhythmia, are followed by compensatory pauses. Each rhythmic radial beat is accompanied in the venous tracing by *a*, *c*, and *v* waves, as seen in the accompanying tracings. At the occurrence of a premature beat a large composite wave is seen in the jugular tracing, occurring at or a little before the expected time of a *c* wave, and also at the expected

instant for the rhythmic auricular wave. The tall composite wave is evidently due to a simultaneous contraction of auricle and ventricle, the ventricular contraction being premature while the auricular contraction belongs to the normal series of such beats. The polygraphic pictures are consequently typical examples of premature contractions arising in the ventricle, disturbing the ventricular rhythm, while the auricular rhythm remains undisturbed.

Electrocardiographic curves show the same events quite clearly. Examples of the three leads are shown in Figs. 4, 5, and 6. In each of these curves two or three premature beats are seen. In lead *I* (Fig. 4) there are three such beats. They resemble the normal ventricular beats except that *R* is shorter, *S* deeper, and *T* somewhat taller. The rhythmic auricular contraction falls in

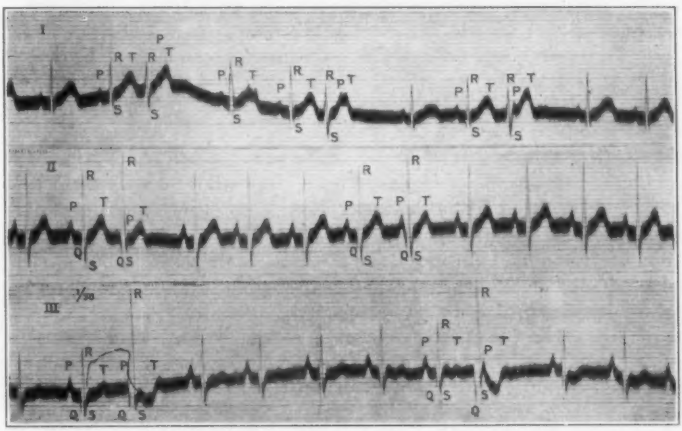


FIG. 4

FIG. 5

FIG. 6

FIGS. 4, 5, and 6.—Electrocardiograms from the same case showing the three leads: lead *I*, from right arm to left arm; lead *II*, from right arm to left leg; lead *III*, from left arm to left leg.

each instance on the upstroke of *T*, but the relation of the buried *P* summit varies somewhat in relation to the apex of *T*, being near its summit in the central disturbance and near its onset in the last disturbance. In lead *II* (Fig. 5) there are two premature beats. The ventricular complexes of these beats have a similar form to the rhythmic beats except that *R* is taller and *Q* is deeper, while *T* is somewhat reduced. The sequential auricular contraction falls with *S* in the case of the first premature beat. In lead *III* (Fig. 6) there are two premature beats, the ventricular complexes of which have tall *R* summits, deep *Q* deflections, and inverted *T* summits, as compared with the sequential beats. The sequential *P* falls directly before and with *Q* of the first premature beat, and with and directly after *S* of the second premature beat.

The electrocardiograms therefore show the ordinary events as they are recognized in premature ventricular contractions so far as the relationship of separate auricular and ventricular contraction is concerned. The peculiarity of the curves lies in the resemblance between the ventricular complexes of the premature beats and those of the rhythmic beats of the same case. This resemblance is so close that the premature beats can only have arisen in impulses which have passed along the normal channels of conduction which join auricle to ventricle. They are beats which are known to be of supraventricular origin, meaning by this term beats propagated from impulses arising above the level of the main division of the auriculoventricular bundle. The minor alterations in the shapes of the complexes in the three leads, changes which have been already described, are not incompatible with this view, for similar changes are known to occur when premature beats arise in the auricle. The changes result from prematurity, and in a measure are comparable to those which are seen with changes of heart rate; they have been described with other phenomena of a similar character under the term "aberration."

The premature beats of the present case, though arising above the main division of the bundle, have not interfered with the sequential contractions of the auricle; it may consequently be presumed they have arisen at a lower level than the main mass of auricular tissue; in other words, either in the auriculoventricular node or in the main bundle itself. If these beats arose in the auriculoventricular node we should anticipate simultaneous contractions of auricle and ventricle propagated from this point. But, as a matter of fact, and as the curves show, synchronism of contractions when it does occur is a coincidence, for the auricular beats evidently originate in the normal impulse centre, the sino-auricular node, while the ventricular beats come from an extraneous point.

There seems only one possible objection to the interpretation of these contractions as having their origin in the bundle itself. If they arose in the auriculoventricular node at such instants that the impulse sent back to the auricle always found this chamber in the refractory state. then the auricle would not contract in response to the nodal impulse and the synchronism of the auricular and ventricular beats might be readily explained. But, as a matter of fact, this explanation will not suffice in the case of the present figures. If we take the time for the retrograde impulse at the same length as the *P-R* interval, then in the case of Fig. 4 the impulse of the central premature beat should have reached the auricle before it contracted in response to the impulse from the pacemaker; on the other hand, allowing the same interval, the retrograde impulse would not reach the auricle in the case of the last premature beat of Fig. 5 until the sequential auricular systole was completed.

And it is a matter of indifference what length of time is allowed for the retrograde impulse, for whatever the length the explanation of the transmission of such impulse would break down in the case of one or other of the premature beats considered. We are therefore forced to the conclusion that the premature contractions arose at a point so far distant from the auricle that (as in the case of the interpolated ventricular contractions) no impulses are sent backward to the auricle. Presumably such a point is to be found at a lower level than the auriculoventricular node, and, as we have already concluded from the shape of the premature ventricular complexes that they arose above the level of the main division we must perforce locate the point of origin in the main stem of the bundle.

Another example of beats of the same sort, though perhaps the instance was less clear, was described in the *Quarterly Journal of Medicine*, October, 1911, v, p. 1, No. 17.

Summary. An instance of premature contractions is described in a child, aged four and a half years; the point of origin of the beats was probably to be located in the main stem of the auriculoventricular bundle.

THE PROBLEM OF THE ALIEN INSANE.[1]

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A definition of the word "problem" is "a matter difficult of solution or settlement." Certainly in the latter sense it is difficult of settlement if not of solution, and the question of the alien insane may be considered a problem.

Nowhere in the civilized world does so anomalous a condition exist as regards the insane as in the United States, due in the main, as we shall see, to the inadequacy of the Federal laws, both as to the admission of immigrants and the deportation of insane aliens. Five years' actual residence at least, from the date of admission into this country are required before an alien can become a citizen, yet the law as to his deportation, even though he has never given any evidence of a desire to become a citizen; even though he be incurably insane; even though he is a public charge, says, under Subdivision 3 of Rule 22 of the Department of Commerce and Labor, Bureau of Immigration and Naturalization, that the State of New York must present an application which, among other

[1] Read at the Two Hundred and Forty-ninth Regular Meeting of the Society of Medical Jurisprudence of New York City, Monday, December 9, 1912.

things, shall be accompanied by a medical certificate containing the following:

"(*a*) An explicit statement that the alien is a public charge, where and how, and, if in an institution, the date of admission thereto.

"(*b*) A full and accurate statement of the alien's disabilities, mental or physical; also whether or not a complete cure is possible; and if yes, when; and if not, whether partial cure may be expected; and to what extent the alien will thereafter be self-supporting. Also, in insane cases, recovered or apparently recovered from the attack, whether new attacks are to be expected.

"(*c*) Whether or not the disabilities described constitute the sole causes why the alien is a public charge; any other causes to be stated.

"(*d*) Whether the causes which render the alien a public charge existed prior to landing or arose subsequent thereto, and in the former case the reasons in detail justifying such a conclusion.

"Where the bureau so directs, the application must be further accompanied by a complete copy of the clinical or general history of the case as shown by the hospital records, including the statements of relatives and friends. If deemed advisable by the local immigration officer, it may be further accompanied by the certificate of an officer of the Public Health and Marine Hospital Service in relation to the alien's condition."

This rule is based upon the immigration laws of the United States, which further provide that the alien *may not be deported at all* if he has been in this country for a period of three years or more, the State of New York being then obliged to care for this alien for the rest of his natural life, notwithstanding the possible as well as probable fact that he may not have been a resident of the State but a very short time. In short, while it takes five years for an alien to become a citizen, he can, by being within the borders of the United States for three years, and at no time in any way contributing to the support of the Commonwealth, be in a position to compel the State of New York or any other State to maintain him during the remainder of his life.

The ordinary procedure, as we can readily see, makes it fairly difficult for the State of New York to rid itself of undesirable aliens, even when a common-sense point of view is taken of the meaning of the law. It seems, however, that it was not sufficiently difficult in the eyes of the Department of Commerce and Labor, so a rule was promulgated known as "Decision No. 120." This decision was rendered by Charles Earl, solicitor of the Department of Commerce and Labor, January 11, 1912; later (February 3, 1912) approved by Attorney-General Wickersham. The history of this decision is to be found in the report of the Bureau of Deportation for the year ending September 30, 1912, and in brief is as follows:

"The decision referred to an insane alien at the Manhattan State Hospital who has been certified to by this bureau as becoming a public charge on account of insanity. The certificate set forth that her mental disease resulted from causes existing prior to landing, such causes being constitutional psychopathic tendencies, mental instability, and deficiency, and was endorsed by a passed assistant surgeon of the Public Health and Marine Hospital Service, who certified that in his opinion the patient was insane from predisposing causes existing prior to landing, and that his opinion was based upon a careful examination of the alien, the history of the case, and the records on file at the institution. Furthermore, an independent examination on the part of the Commissioner of Immigration at Ellis Island by a lay immigrant inspector corroborated the details of the history, and, as the result of the combined examination on the part of the passed assistant surgeon of the Public Health and Marine Hospital Service, the medical members of this bureau and the lay immigrant inspector attached to the immigration station at Ellis Island, the Commissioner of Immigration recommended the deportation of this alien in accordance with the laws. The honorable solicitor who, we are led to believe, can make no claim to either any general medical education or any knowledge of what pertains to the diagnosis of mental incapacities, examined the same medical records and the testimony of the various alienists, both State and Federal, and arrived at the conculsion that "neither the history of the case nor the hospital records as presented to the department contained any reference whatever to *causes existing prior to landing*, giving rise to the alien's present insanity.

"That the statement that the alien's insanity is caused by constitutional psychopathic tendencies or mental instability, or other predisposing causes existing prior to landing, is given in the form of a bald medical opinion or conclusion, unaccompanied by any facts or reasons showing on what it is based.

"That there is not an affirmative fact in the record, including the family history and the hospital history of the alien, tending to show either that the alien exhibited constitutional psychopathic tendencies and mental instability at the time of landing or prior thereto, or that such constitutional psychopathic tendencies, or mental instability, or other predisposing causes likely to lead to insanity, could by any known means have been detected at that time.

"That in view of this wholly negative aspect of the evidence, it must be assumed that the medical opinion concerning the underlying insanity and the prior existence thereof is wholly *ex post facto*, because the alien has become insane; the alien was a person of constitutional psychopathic tendencies and mental instability; and because the alien was such a person when insanity developed, the alien was such a person at all prior times.

"That in many cases, as in this, some circumstances or event in the life of the alien since landing affirmatively appear from the evidence, suggesting to the ordinary mind an adequate cause to account for present insanity, independently of any constitutional psychopathic tendencies or mental instability on the part of the individual, *e. g.*, as the account in the present case of a sexual assualt upon an ignorant sixteen-year-old girl in her own home, and the ensuing shame and worry on her part."

As a matter of fact, there was no record whatever of sexual trauma in this case, and the parents, the relatives, and friends of the alien positively denied that any such occurrence had ever taken place. Here we have the most remarkable position taken by a great department of the Federal Government, in which, from a medical standpoint at least, an uneducated, inexperienced, and entirely incompetent person undertakes to overrule, in a most nonchalant and matter-of-fact manner, the carefully considered opinions of the medical superintendent of a State hospital, a man of national reputation as an alienist; the chief of the Bureau of Deportation, whose experience in examining the mental conditions of aliens is not inconsiderable; a passed assistant surgeon of the Public Health and Marine Hospital Service, a service which claims to number among its members men of no small scientific attainments, and the Commissioner of Immigration at Ellis Island. As a result of this very remarkable position taken by the Attorney-General of the United States, not only was the State of New York compelled to return this insane alien to a State hospital, but it is compelled to maintain her for so long as she may remain insane, which, it is believed, will be for the rest of her life. In addition, this decision was printed by the Department of Commerce and Labor and spread broadcast among the steamship companies and immigration officials, and used as a basis for the cancellation of a great number of warrants issued by the New York State authorities. In fact, the department seems to lose no opportunity for treating with open contempt the medical opinions presented to it.

That I may not seem to be speaking without warrant of fact, let me give an example (and here I quote from the report of Doctor Campbell, of the Bureau of Deportation, mentioned before).

"A case of dementia præcox of the paranoid type was certified to by the medical superintendent of that hospital (Gowanda State) on the grounds of constitutional psychopathic tendencies, mental instability, and deterioration. Upon the recommendation of a lay inspector the Department of Commerce and Labor cancelled the warrant of arrest. Upon a request to the Department of Commerce and Labor by this bureau for an examination by a qualified medical officer of the Public Health and Marine Hospital Service, the following decision of the Commissioner of Immigration was received through the Hon. John H. Clark, under date of October 3, 1912:

"'It is noted that Dr. Campbell requests that a properly qualified medical officer of the Public Health and Marine Hospital Service be assigned to reëxamine the above-named alien with a view to her deportation. You are requested to advise Doctor Campbell that such a proceeding is deemed impracticable and unnecessary, as it is considered that this case has received the most careful attention, and the facts relating thereto were thoroughly investigated before arriving at a decision. The matter is therefore closed so far as the bureau is concerned.'"

In case, however, that the State authorities are fortunate enough to have surmounted these various stringent rules, they must still bear the expense of maintenance of the alien for a considerable period, as provided for in this Subdivision 3 of Rule 22 of the Department of Commerce and Labor:

"The cost of maintaining aliens during these proceedings may be borne by the Government, but as to aliens who have become public charges from causes existing prior to landing, such cost will be allowed only for the period subsequent to the date of issuance of warrant of arrest, and then only in case this is followed by an order of deportation. Maintenance bills under this rule shall be delivered to the immigration officer in immediate charge of the case within twenty days from the close of the calendar month in which occurs the death of the alien or removal from the institution for deportation, and failure so to render them shall relieve the United States from any responsibility for the payment thereof. If proceedings against a procurer or contractor are instituted (Sections 3, 5, or 20), immigration officers shall report to the United States District Attorney the amount of the cost of deporting the alien, including one-half of the entire cost of removal to the port of deportation, so that a proper effort may be made to recover such expense from the procurer or importer and the reimbursement of the Government and the transportation company for their respective parts thereof."

When deportation was first undertaken the State was reimbursed from the day of the admission of the alien into the State hospital, which, it would seem, was a most just proceeding if the alien was improperly in the State of New York. This custom, however, was soon modified, and the State was reimbursed from the time that the Department of Commerce and Labor was notified that a deportable alien was in the hospital. Still another modification was later made, and the State was reimbursed from the time the State authorities were able to verify the landing of the alien in this country. As we have seen, it is now so arranged that the State is reimbursed only from the time that the warrant of arrest is issued, a matter of sometimes but a few days, while the time elapsing from the notification to the Federal Government by the Bureau of Deportation of the presence of an insane alien

in this State may be several months. And yet even though this alien be subsequently deported under Federal warrant, the State of New York must continue to maintain him instead of the Federal Government.[2] Under the first method of procedure mentioned the moneys received from the United States Government for the reimbursement of this State more than paid the expenses of the Bureau of Deportation, but now the amount so received is but a trifle.

Before further considering the subject of deportation, it may be wise to take up the general proposition as to the whole number of insane in the State, the number of foreign born and the number of native born, the number of aliens, and the relation which the latter bear to the former, as well as to the methods employed, both at the ports of emigration and immigration, to prevent the entry of mental defectives into the United States.

The statistics which are now presented are based upon figures obtained from the New York State Hospital Commission, and not upon data collected by this Commission. This statement is made for the reason that in the report which will be submitted at a later date, the figures which will be given will not correspond exactly with those which are given here, for the reason that the statistics gathered by the State Hospital Commission were not especially directed toward the question under discussion, but had for their main proposition the nativity rather than citizenship, while the statistics which this Commission is now gathering, and which will be explained farther on in this paper, are based upon both nativity and citizenship. It might be further added that the estimates as to cost of maintenance and as to actual numbers of aliens in the tables in this paper are smaller than the figures which will be submitted in the future report.

In February, 1912, there were in the State Hospitals for the Insane 32,662 patients. Of these, 17,853 were native born and 13,163 were foreign born, or, roughly speaking, 45 per cent. were of foreign birth. Of these a large proportion were aliens, but the exact number it is impossible to state.

"In 1900[3] the foreign born constituted 26 per cent. of the total population of the State, and in 1910, 29.9 per cent." (These are census periods.) "The foreign-born population of the State therefore contributes relatively a larger number of patients to the State Hospitals than the native population. The ratio of relative contribution to the civil hospitals in 1903 was 2.44 to 1, and 1912, 1.69 to 1. As children below the age of fifteen years rarely become

[2] See Rule 22 of Department of Commerce and Labor, Bureau of Immigration and Naturalisation, November 15, 1911, third edition.

[3] See A Statistical Study of the Foreign-born Insane in the New York State Hospitals, by Horatio M. Pollock, Statistician, State Hospital Commission, New York State Hospital Bulletin April, 1912, p. 10.

insane, a part of the relatively large contribution of foreign-born patients to the State hospitals is due to the fact that the immigrants, when they come to this country are largely between the ages of fifteen and forty years, and therefore contain a relatively larger number of adults than the native population. As an offset, however, to the relatively greater number of adults among the foreign born is the relatively greater number of persons of advanced age among the native born. No statistics of the age distribution of the population of the State at the time of the 1910 census are available. It is therefore impossible to calculate just what allowance should be made in determining the relative frequency of insanity among the foreign born.

"The study made by the Federal Census Bureau in 1914 showed that the relative frequency of insanity among the foreign born in the various States differed in accordance with the nationalities composing the foreign-born population. Taking the country as a whole, however, the foreign born, which in 1900 formed only 19.5 of the total population of ten years of age and over, contributed 34.3 per cent. of the insane. A closer comparison of the relative frequency of insanity among nationalities will be found in the analysis of first admissions for New York City.

"The nationality of the insane population in the State varies as the tide of immigration shifts from one section of Europe to another. Until recent years the greater part of the immigrants settling in New York State came from Ireland and Germany. During the past decade these people have practically ceased to immigrate, but instead large numbers have come to the State from Austria-Hungary, Russia, and Italy."

Doctor Pollock says that relatively there has been a decrease in the insane population from Ireland, Germany, England, and Wales, and an increase in the insane population from Russia and Poland, Italy, and Hungary and Bohemia. (See Chart I.) The Census Bureau's report of 1904 did not give separately the number of patients born in Austria. This country now contributes 4.5 per cent. of the population of the civil hospitals and 5.3 per cent. of the population of the hospitals for the criminal insane.

On Chart II, which relates to the increase of native-born and the increase in foreign-born insane in New York State as compared with the general population, in their respective classes, the most striking fact is that during the period from 1900 to 1910 (which years are taken as a basis because they are census periods) the increase in the native-born population was 18. 4 per cent. as against 44.4 for the foreign, and yet the increase in native-born patients in the civil State hospitals was 35.7 per cent. while the foreign born was 18.5. On the face of it this would indicate that the insanity rate among the foreign born was decreasing as compared with the native born; but if we go a little farther we will see that

during practically this same period, or from 1903 to 1912 (which dates are taken because they approximate the census dates and are the only figures at present available), the State authorities, through the Bureau of Deportation, deported and repatriated or

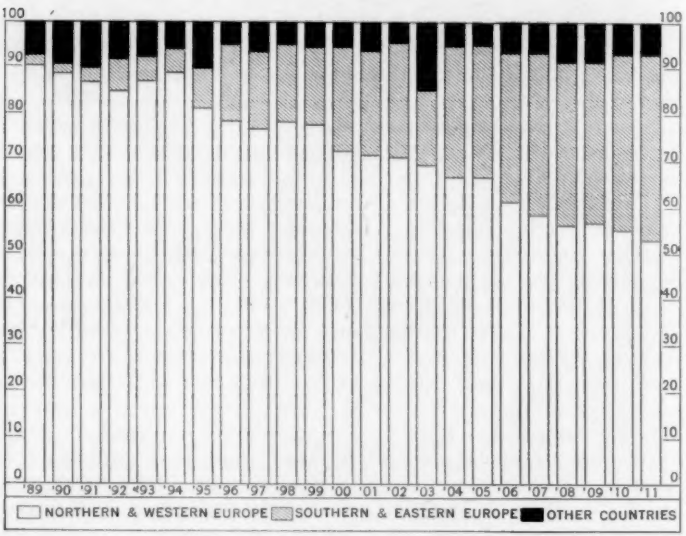

CHART I.—Percentage of patients born in different sections of Europe admitted annually to the New York State hospitals, 1889 to 1911.

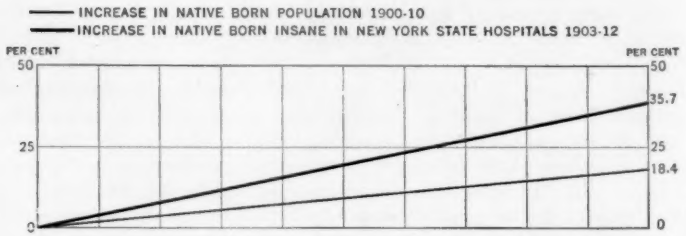

CHART II.—Increase of native-born population compared with increase of native-born insane in New York State hospitals, 1903 to 1912.

returned to their homes, 4,648 patients. And of these the probable number who would have remained in the State hospitals on May 12, 1912, is 3350, making the total of foreign born 16,695, or an increase since 1903, of 48.3 per cent. in the foreign born as against 35.6 per cent. native born.

Memoranda to accompany charts relative to increase of native-born and increase of foreign-born insane in New York State compared with the general population in the respective classes.

NATIVE WHITE POPULATION OF NEW YORK STATE.

	Number.	Per cent. of total.
1900	5,267,358	72.5
1910	6,237,661	68.4

Increase, 18.4 per cent.

FOREIGN WHITE POPULATION OF NEW YORK STATE.

	Number.	Per cent. of total.
1900	1,889,523	26.0
1910	2,729,260	29.9

Increase, 44.4 per cent.

PATIENT POPULATION OF CIVIL STATE HOSPITALS.

	Native born.		Foreign born.	
	Number.	Per cent.	Number.	Per cent.
December 31, 1903	13,110	53.1	11,258	46.9
May 6, 1912	17,792	56.4	13,345	42.3
Per cent. of increase	.....	35.7	.....	18.5

Number of foreign-born insane deported and returned to their homes from 1903 to May 1912, 4648.

Probable number of these who would have remained in the State hospitals, May, 1912, 3350, making the foreign-born total 16,695 and the increase since 1903, 48.3 per cent.

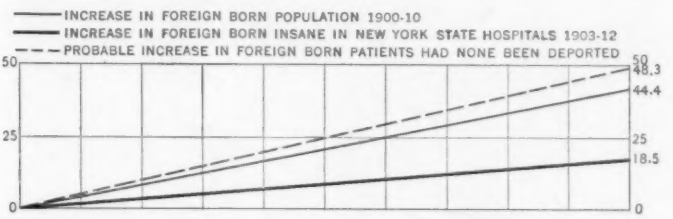

CHART III.—Increase in foreign-born population compared with increase in foreign-born insane in New York State hospitals, 1903 to 1912.

In computing the number that would have remained in the State hospitals at the time of the census of May 6, 1912, it is assumed that the average complete hospital life of a foreign-born patient is eleven years, and that the number of those deported who would have left the hospitals before the time of taking the census bears the same relation to the whole number deported during the year, as the number of years elapsed since deportation bears to eleven. In other words, it is assumed that an equal number of discharges is made during each year. While the result obtained by this method is only an approximation, it may fairly be considered as indicative

of the probable result. The figures for the different years, with the fraction still remaining, are shown in the following tabulation:

Year.	Total foreign born returned to homes.	Fraction remaining May, 1912.	Probable number in hospitals Feb. 10, 1912, had none been returned.
1903–4	201	$\frac{3}{11}$	55
1904–5	334	$\frac{4}{11}$	121
1905–6	336	$\frac{5}{11}$	153
1906–7	403	$\frac{6}{11}$	220
1907–8	476	$\frac{7}{11}$	303
1908–9	539	$\frac{8}{11}$	392
1909–10	689	$\frac{9}{11}$	562
1910–11	887	$\frac{10}{11}$	801
1911–12, app.	785	$\frac{125}{152}$	743
	4648		3350

These figures are not quite correct, as they are not based upon absolutely accurate data, but the number of aliens in the corrected tables will be found to be, we are quite confident, greater than here given.[4]

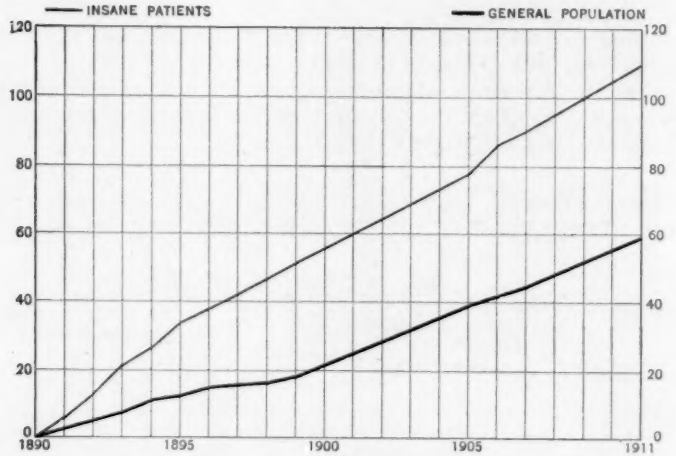

CHART IV.—Increase of insane patients in all institutions in New York State, compared with increase of population, 1890 to 1911.

It is estimated by the statistician of the New York State Hospital Commission, Doctor Horatio M. Pollock, that the cost of maintenance per annum for patients in the State hospitals averages $262 per year, and that the total cost of maintaining an average patient is $2282; so that the estimated cost to the State of New York

[4] Chart IV gives a graphic illustration of the increase in the insane population of State institutions compared with the increase of general population, 1890 to 1911.

(excluding the hospitals for the criminal insane and King's Park and Binghamton, which latter collectively have a population of 5800, but for which no figures are now available) for the aliens in the State hospitals on September 30, 1911, if they live out their expectancy, would be approximately $10,000,000, and this refers only to the aliens *now* in the hospitals.

Recognizing the serious economic factor to the State, the Legislature, at the suggestion of former Governor Benjamin B. Odell, Jr., created in 1904, what was then called the State Board of Alienists, and what the last Legislature (1912), with the approval of Governor Dix, has called more properly the Bureau of Deportation.

Chart V shows the number of aliens deported from September 30, 1903, to September 30, 1912, by years, as well as the economic saving effected each year. During the first year of the bureau's existence it will be noted that 176 aliens were deported; that there has been a gradual rise in the number deported (and when the word "deported" is used repatriation is also included) each year up to and including the years 1910 and 1911, and that during the period of 1911 and 1912 there is an increase of almost 400, and that the total economic saving to the State during that period by this department of the State Hospital Commission has been $10,590,925. These figures as to cost are arrived at in the following way:

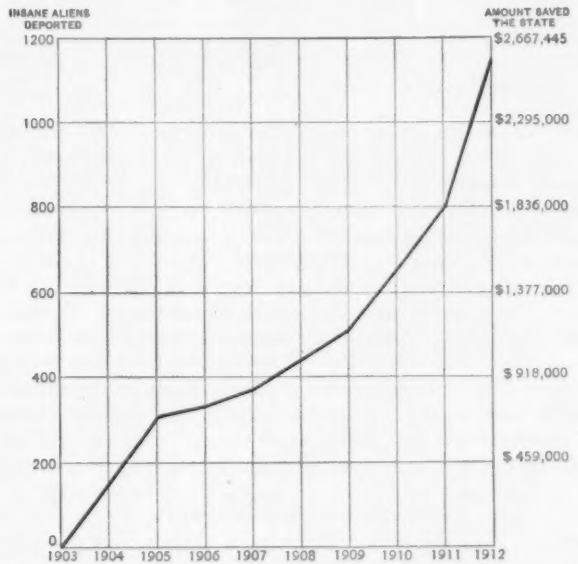

CHART V.—Insane aliens deported by State Hospital Commission with economic savings effected, 1903 to 1912.

Memoranda to accompany chart relative to insane aliens deported by the State Hospital Commission with economic saving effected 1903–12.

The annual cost of maintaining a patient in a New York State hospital averages $262 per year. This amount is made up of three elements, as follows:

Hospital care, including food, clothes and treatment	$188
Investment charge, including interest on cost of building and depreciation	70
General supervision, including the expense of the State Hospital Commission, the Bureau of Deportation, and the Psychiatric Institute	4

The average hospital life of a patient is approximately eleven years. The total cost of maintaining the average patient is $2882. In case a patient is deported soon after admission the saving to the State would be the present worth of $262 expended annually for eleven years. This is found to be $2295. Therefore the economic saving resulting from deportations of alien insane each year, since the beginning of the fiscal year of 1903, is as follows:

Year.	Alien deportation.	Economic saving effected.
1903–4	176 × $2295	$403,920
1904–5	299 × 2295	686,205
1905–6	307 × 2295	704 565
1906–7	352 × 2295	807,840
1907–8	424 × 2295	973,080
1908–9	489 × 2295	1,122,255
1909–10	613 × 2295	1,406,835
1910–11	784 × 2295	1,799,280
1911–12	1171 × 2295	2,687,445
		$10,590,925

Later on in this paper the methods employed for deportation and repatriation, as well as the difficulties encountered by the Bureau of Deportation, will be considered.

The total estimated capacity of the civil State Hospitals for the Insane on September 30, 1911, as certified by the various hospital superintendents, was 21,276. The total population on that date, we will see, was, without including the hospitals for the criminal insane or King's Park and Binghamton, 25,643. The overcrowding on the particular date was 4367. The number of aliens on that date was 4461. If we deduct from the total population the number of aliens, instead of being overcrowded 4367, it can be readily seen we will have room and to spare for several years to come for our native-born insane. An example of this overcrowding may be seen if we take the figures of one hospital:

MANHATTAN STATE HOSPITAL.

Capacity	3596
Population	4702
Overcrowded	1106
Aliens	1905

It must be remembered that there are two hospitals for the insane criminals, the figures for which are not here included. It is unfortunate that we are unable to give more accurate figures, but we have been unable as yet to obtain full data as to Binghamton and King's Park.

A more interesting factor than the question of cost of maintenance, a more serious phase of the problem than the mere question of money, the question of heredity, will be seen by reference to Chart VI, which is based upon nativity and parentage of first admissions to the State hospitals for the year ending September 30, 1911.

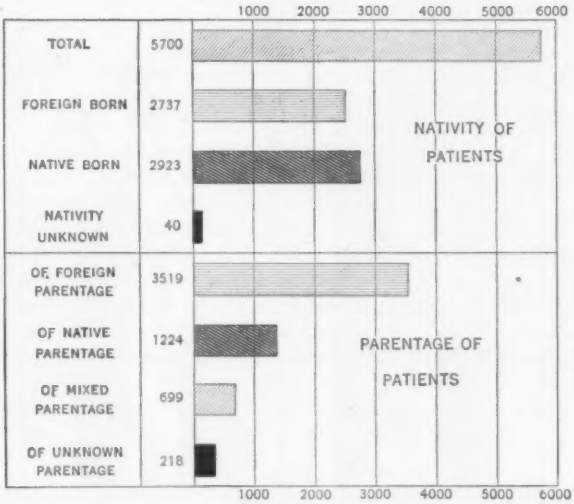

CHART VI.—Nativity and parentage of first admissions to the State hospitals, year ending September 30, 1911.

Memoranda to accompany chart on nativity and parentage of first admissions to the State hospitals for the year ending September 30, 1911.

Total first admissions to the State hospitals, 5700. Of these 2737 were foreign born, 2923 native born, and 40 of unknown nativity.

The foreign born first admissions constitute 48.36 per cent. of the total number of those whose birthplace was ascertained.

The parents of 3519 of the 5700 first admissions were foreign born and of 1224 native born. 699 first admissions had mixed parentage, *i. e.*, one parent was native born and the other foreign born, or one parent unknown and the other either native born or

foreign born. The parentage of 218 of the patients was unknown. The patients whose parents were of either foreign or mixed parentage constituted 74 per cent. of the whole. If only the patients whose parentage was ascertained were considered, those having foreign and mixed parentage constitute 76.9 per cent. of the whole. The first admissions with both parents of foreign birth constitute 64.2 per cent. of the patients the nativity of whose parents was ascertained.

The most prevalent psychosis is a matter of some interest to us, from both the eugenic and the financial standpoint. As testified

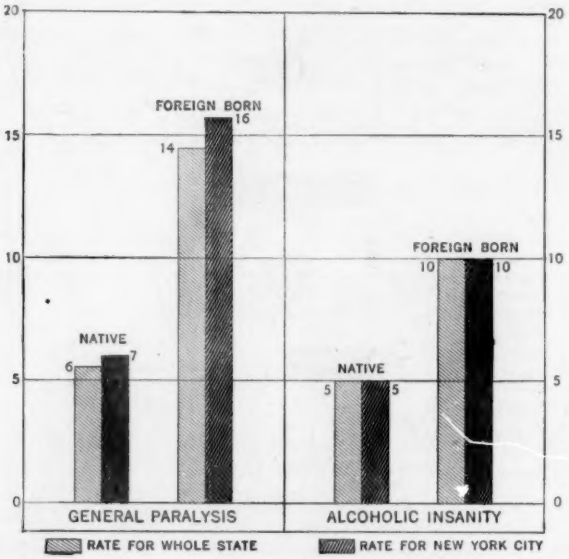

CHART VII.—Rate of frequency of general paralysis and alcoholic insanity per 100,000 of population, first admissions, 1911.

to by the various hospital superintendents, and by reference to the statistics of the State Hospital Commission, we are informed that the most prevalent psychosis is what is now generally known as dementia præcox, the second general paresis, and the third alcoholic dementia. Chart VII gives an illustration of the relative frequency of general paresis and alcoholic insanity among the native born and foreign born. There is no chart to show the relative frequency between the native born and foreign born as to dementia præcox, the testimony of the hospital superintendents indicating that the difference is immaterial. It will be seen here that there is a far larger rate of general paresis and alco-

holic insanity among the foreign born than among the native born when we consider the greater native-born population. There is an additional factor here which should attract our attention, and that is that a large proportion of the patients admitted to our hospitals of foreign birth are young adults, most of them in an otherwise healthy condition, while the admissions for the native born cover all ages up to and including very old age. In these three psychoses it is no uncommon occurrence for a patient to have a lucid interval of a considerable length, during which time he is discharged from the hospital, and many of these patients marry and have offspring to whom, of course, is transmitted an hereditary taint, which may, in a considerable measure, account for the fact that the percentage of those having both parents of foreign birth is considerably greater than those having both parents native born.

Memoranda to accompany chart relative to frequency of general paresis and alcoholic insanity among the native born and foreign born.

General paresis and alcoholic insanity are of special significance on account of their being due to faulty methods of living. Among the 5700 first admissions to the State hospitals for the year ending September 30, 1911, there were 758 cases of general paresis and 580 cases of alcoholic insanity. Comparing the number of cases with the general population, classified with respect to nativity, we find that in general paresis the native born of the State at large had 6 cases per 100,000 and the foreign born 14 per 100,000. Taking the population of New York City alone, we find that there were 7 cases of general paresis per 100,000 of population among the native born and 16 cases among the foreign born. The rates of alcoholic insanity both of New York City and for the whole State were 5 per 100,000 among the native born and 10 per 100,000 among the foreign born.

An examination of the immigration officials and the representatives of the various steamship companies entering the port of New York throws a clear light upon the reason for this enormous burden of mental incompetents which this State, more than any other State in this country, is obliged to bear. Various methods are employed at various points of embarcation. In some parts of southern Europe stations are maintained which are called "control stations," where the intending immigrant is examined by officials of the country from which they come and by steamship officials to ascertain if they come within the requirements of the Federal law. In addition to this they are examined again in the same manner upon the wharf of the steamship company before embarcation. In England there is but this one examination, which is conducted upon the wharf of the steamship company or upon a lighter which carries the immigrant to the ship. In Italy the examination is made at the various ports by an official

of the Italian Government, in some instances assisted by (through the courtesy of the Italian Government) an officer of the United States Public Health and Marine Hospital Service. The value of this examination as to the detection of mental incapacities or psychoses may be readily seen when we are told that the immigrants from southern Europe are examined frequently at the rate of about 600 per hour, or 10 per minute; that the English immigrants are examined during the time required for the barge to go from the landing-place to the ship, which means that from 200 to 600 are examined in about half an hour, or from 7 to 21 per minute; and at the Italian ports (where it is claimed the examinations are the most thorough of any of those made at the ports of emigration) the lowest rate given is 200 per hour and the highest rate 400 per hour, or about 3 to 6 per minute. We are further told that these patients are under observation during their journey from the port of emigration to Ellis Island, but that no special examination is made as to their mental condition. As to what happens at Ellis Island, let me quote from an address of the Hon. William Williams, United States Commissioner of Immigration, before the Mental Hygiene Conference at New York City, November 14, 1912, in which address he says:

"I shall refer only to the detection of the mental diseases with which immigrants may be afflicted, and shall show how inadequate are the ways and means which Congress has provided therefor. I am one of those who believe that the Legislature does only half its duty when it enacts a good law. The other half is to furnish adequate machinery and ways and means for its execution, without which the law accomplishes only a part of its purpose, and is there to perplex executive officials whose sworn duty and desire it is to execute it.

"Immigration to this country is at a very heavy rate. In round numbers it has, during each of the past ten years, averaged 900,000 annually, and the great bulk of it has been through Ellis Island. Only last month there arrived at New York over 80,000 aliens, an average of nearly 2600 a day. Nor are the arrivals evenly distributed over the days of the months, on the contrary there arrive, sometimes for several days in succession, 4000 or 5000 a day. A great many of these people come from the poorer classes of the poorer countries of Europe. Their general physical condition is often far from good and their ignorance beyond belief. Not only are many illiterate, but many do not know the days of the week, the months of the year, their ages, or any country in Europe outside of their own. These people speak many strange tongues and dialects, and interpreters familiar with approximately forty are necessary to enable the Government authorities to converse with them. A number of those who are undesirable additions to our population are nevertheless admissible under the low requirements of existing law. Obviously the task of picking out from among

this heterogeneous mass those suffering from any mental disability is a gigantic one. It would be impossible of complete performance even if the medical staff were in size what it should be. But Ellis Island has to transact its heavy business with the instrumentalities and facilities which Congress provides. It has in all 650 officials. Of these about 130 belong to the Public Health Service, which number includes all medical officers (doctors), hospital attendants, and nurses. The medical officers number only 21, far too few, for they have to perform a multitude of duties in relation both to the inspection of the masses of immigrants who arrive and the care of those detained in the Ellis Island hospitals for sickness, such sick numbering at times several hundred.

"The process of medical inspection is roughly this: Each immigrant passes before two medical officers who rapidly look him over with a trained eye and set aside for special examination all who bear any indications of physical or mental defects. Those so set aside are, for the purposes of mental examination, subjected to well systematized test questions, which the medical officers have evolved from their own special experience, and they apply also such recent modern and scientific methods as those worked out by Binet-Simon, Fernald, Goddard, and others. All such special cases, of which last year there were about 5000, are gone into very thoroughly and are often detained eight days, or longer, for mental observation. But not enough cases are thus set aside, because the medical officers are compelled to work too quickly and lack the requisite number of interpreters to enable them to converse with each immigrant as he goes by. Furthermore, the space at Ellis Island available for the observation of immigrants suspected to be suffering from mental defects is too small."

And he further states that he has frequently called attention, to these matters, asking for an additional force of inspectors, for better accommodations for the examination of the incoming immigrants, and for various other necessary matters, and that Congress has, to a limited extent only, taken note of these matters. And I should like to say just here that if the Federal Government, as constituted by Congress, were as heartily in accord with providing means for the detection of mental defectives as the authorities at Ellis Island are in the execution of the laws, a large measure of our problem would have been long since solved.

There are two methods by which aliens are returned to their native country. One I have already described to you in an earlier part of this paper as deportation, in which all expenses are borne by the steamship companies. The other is the method which is known as repatriation, and the most remarkable condition connected with the problem of the alien insane confronts us here. The State of New York repatriates annually many more aliens than are deported by Federal warrant, *and yet they are repatriated only upon their own consent and through the courtesy of the various steamship*

of the Italian Government, in some instances assisted by (through the courtesy of the Italian Government) an officer of the United States Public Health and Marine Hospital Service. The value of this examination as to the detection of mental incapacities or psychoses may be readily seen when we are told that the immigrants from southern Europe are examined frequently at the rate of about 600 per hour, or 10 per minute; that the English immigrants are examined during the time required for the barge to go from the landing-place to the ship, which means that from 200 to 600 are examined in about half an hour, or from 7 to 21 per minute; and at the Italian ports (where it is claimed the examinations are the most thorough of any of those made at the ports of emigration) the lowest rate given is 200 per hour and the highest rate 400 per hour, or about 3 to 6 per minute. We are further told that these patients are under observation during their journey from the port of emigration to Ellis Island, but that no special examination is made as to their mental condition. As to what happens at Ellis Island, let me quote from an address of the Hon. William Williams, United States Commissioner of Immigration, before the Mental Hygiene Conference at New York City, November 14, 1912, in which address he says:

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this heterogeneous mass those suffering from any mental disability is a gigantic one. It would be impossible of complete performance even if the medical staff were in size what it should be. But Ellis Island has to transact its heavy business with the instrumentalities and facilities which Congress provides. It has in all 650 officials. Of these about 130 belong to the Public Health Service, which number includes all medical officers (doctors), hospital attendants, and nurses. The medical officers number only 21, far too few, for they have to perform a multitude of duties in relation both to the inspection of the masses of immigrants who arrive and the care of those detained in the Ellis Island hospitals for sickness, such sick numbering at times several hundred.

"The process of medical inspection is roughly this: Each immigrant passes before two medical officers who rapidly look him over with a trained eye and set aside for special examination all who bear any indications of physical or mental defects. Those so set aside are, for the purposes of mental examination, subjected to well systematized test questions, which the medical officers have evolved from their own special experience, and they apply also such recent modern and scientific methods as those worked out by Binet-Simon, Fernald, Goddard, and others. All such special cases, of which last year there were about 5000, are gone into very thoroughly and are often detained eight days, or longer, for mental observation. But not enough cases are thus set aside, because the medical officers are compelled to work too quickly and lack the requisite number of interpreters to enable them to converse with each immigrant as he goes by. Furthermore, the space at Ellis Island available for the observation of immigrants suspected to be suffering from mental defects is too small."

And he further states that he has frequently called attention, to these matters, asking for an additional force of inspectors, for better accommodations for the examination of the incoming immigrants, and for various other necessary matters, and that Congress has, to a limited extent only, taken note of these matters. And I should like to say just here that if the Federal Government, as constituted by Congress, were as heartily in accord with providing means for the detection of mental defectives as the authorities at Ellis Island are in the execution of the laws, a large measure of our problem would have been long since solved.

There are two methods by which aliens are returned to their native country. One I have already described to you in an earlier part of this paper as deportation, in which all expenses are borne by the steamship companies. The other is the method which is known as repatriation, and the most remarkable condition connected with the problem of the alien insane confronts us here. The State of New York repatriates annually many more aliens than are deported by Federal warrant, *and yet they are repatriated only upon their own consent and through the courtesy of the various steamship*

companies entering the port of New York, and through no right of the State whatsoever. Further, they are repatriated entirely at the expense of the State of New York, which first ascertains the willingness of the alien to return, next whether his friends in the country from which he emigrated will provide for him when he is returned; further, that he is in a fit condition to travel; and beyond all this, it is the custom not only to buy his ticket to his own home, but to send with him a nurse or attendant whose expenses are paid by the State of New York, and he is still further provided with a sum of money to place in his pocket on his return home. Thus we see that in order to get rid of the undesirable alien, the State of New York must not only obtain his consent and the consent of the steamship company to return him, but must pay a considerable sum of money for that return.

At present the arrangement with the various transportation companies entered into by the Bureau of Deportation, bearing date November 17, 1912, provides that the various steamship companies entering into this agreement will repatriate such patients as are presented to them by the Bureau of Deportation, as represented by Doctor Campbell, who are in a fit condition to travel, who will return voluntarily, and whose relatives and friends will provide for him on his return to his native land.

Various methods have been suggested as a solution of this vexing problem. The one advanced by the steamship officials is that there should be stationed at the ports of emigration United States officials, who should partake in the examination of the intending immigrant, and who would therefore share the responsibility with the officials of the steamship companies and the foreign government, a remedy which obviously would be a most advantageous one to the steamship companies. Another is that there should be stationed upon each ship bearing immigrants to this country United States officials, either physicians or nurses, or both, who should observe the patients from time to time and segregate those apparently suffering from psychoses. Another is that a larger number of inspectors should be provided for at Ellis Island, and that these inspectors should be men trained in the detection of mental incapacities. Another is the providing for a detention hospital in which suspected cases could be isolated for a longer or shorter period until proper observation could be had as to their mental condition. Still another is that the time during which deportation could be had under Federal warrant should be lengthened to five years, to correspond with the time required to become a citizen. It was suggested, as well, that Decision No. 120 should be rescinded and the testimony of competent alienists as to the mental condition be taken as sufficient authority for the issuance of a Federal warrant, if other conditions admit. Another is that the law, instead of providing that the Federal authorities shall show that the causes for the patient's psychosis existed prior to his landing, should provide

that the alien should show that the causes for his psychosis did not occur subsequent to his landing, putting the burden of proof upon the alien rather than upon the Government. The last, and what seems to be, in the general opinion, the most generally approved suggestion, is that the steamship companies shall be made responsible for the mental condition of the immigrant as they are made responsible for his physical condition—that is, that for each alien brought to this country who develops a psychosis within the five-year period, the steamship companies shall be fined $100 and compelled to return the immigrant to the port from whence he sailed, just as they are to-day fined and penalized in cases of favus and trachoma which they bring to this country.

This commission, known as the Commission to Investigate the Alien Insane, was appointed by the Hon. John A. Dix, Governor of the State of New York, on March 16, 1912, and the information given in this paper was obtained through public hearings held at the various State hospitals throughout the State and at public hearings in the city of New York, at which there have been already taken more than a thousand pages of typewritten testimony. It has been the good fortune of this commission to be able to interest many other States in the same matter, and it has devised two sets of history cards for each patient in the State hospitals, the results of which are now being tabulated, one based upon nativity and the other upon citizenship; and a number of States which have the same problem, only in a lesser degree, have, at the request of this commission, undertaken the collection of identical statistics with those which are being collected in this State. The system which, at the request of this commission, the State Hospital Commission has adopted, and which has been concurred in by the other States which have joined the State of New York in the investigation, is as follows: For each patient in the hospitals for the care of the insane in this State there is a history card, based upon both nativity and citizenship, as will be seen by an examination of the card.

Nativity and Citizenship

.. ..State Hospital

First Admission Male

Name ..... Identification No.....

Nativity (county of birth) of patient .....
Nativity (county of birth) of father .....
Nativity (county of birth) of mother .....
Citizenship of patient American Foreign
If naturalized, how? By final papers By naturalization of parents
Citizenship of father American Foreign
If naturalized, how? By final papers By naturalization of parents
Was father a citizen at time of birth of patient?.....
Time of patient in U. S. before admission.....Years.....Months
Total time of patient in State hospitals for insane.....Years.....Months
Date of admission.....19.....

First admission cards are printed on white card-board and readmission on salmon, male with black ink and female with red. And of course the female card differs from the male card in regard to the naturalization questions. In the case of readmissions another card is made similar to the first card, so that first admissions are always kept distinct from readmissions and there is no reduplication. In the investigations of this commission it was found that various interpretations had been placed upon questions asked of different hospital superintendents, and it was thought wise to issue with the history card a circular of information which should define carefully every question asked. This circular of information reads thus:

STATE OF NEW YORK—STATE HOSPITAL COMMISSION.

EXPLANATIONS AND INSTRUCTIONS RELATIVE TO NATIVITY AND CITIZENSHIP CARDS.

The nativity and citizenship cards are to be filled out for all patients (exclusive of transfers) admitted to the State hospitals each year from 1905 to 1912 inclusive.

First admissions should be kept separate from readmissions and males from females. The cards of each year should also be kept separate from those of other years.

First admission cards are printed on white card-board and readmission on salmon, male with black ink and female with red.

The *name* of the patient should be given in full.

In reporting the nativity the United States census classification of countries should be used as a guide. If in any case the country of birth can not be ascertained, state whether person is foreign or native born.

The *citizenship* of the patient and of the father of the patient should be definitely reported as American or foreign. Foreign-born persons are considered aliens unless naturalized, and their citizenship should be reported as foreign *if evidence of their naturalization cannot be produced.*[5]

Aliens may be naturalized in several ways, as follows:

1. By making required declarations and receiving final naturalization papers from a court of competent jurisdiction.

2. A woman by the naturalization of her husband or by marriage to a citizen.

3. Minors by the naturalization of their parents.

A child born in the United States is a citizen regardless of parentage.

A woman loses her citizenship by marriage to a foreigner.

A declaration of intention does not confer rights of citizenship; a foreigner is an alien until actually naturalized. An alien, to be eligible for citizenship, must have resided in the United States continuously for five years.

The *time spent in the United States* before admission or readmission should be given definitely in years and months. The time spent by the patient in State hospitals for the insane should include all admissions, and, in case patient is still in hospital, should be reckoned to September 30, 1912.

Cards, when filled out, should be forwarded to the State Hospital Commission.

Among the States which have undertaken a similar inquiry are the following: New Hampshire, Connecticut, Massachusetts, Rhode Island, New Jersey, Pennsylvania, Maryland, Indiana, Illinois, West Virginia, South Carolina. Heretofore there has been a lack of uniformity in statistics relating to the insane and I know of none published relating to citizenship, both of which wants are supplied by the adoption of these cards by these various States. It is the intention of this commission, when the full and complete data is collected, to call a public meeting in the city of New York of the representatives of these various States and of other individuals and organizations interested in the matter, to discuss ways and means for a solution of this problem.

[5] A foreign-born person whose parents are citizens of the United States is not an alien.

COMBINED TUBERCULOSIS AND CARCINOMA OF THE STOMACH, WITH A REPORT OF A CASE UPON WHICH A PARTIAL GASTRECTOMY WAS PERFORMED.[1]

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The present consensus of opinion regarding the coexistence of tuberculous inflammation and cancer coincides with that put forward by Bayle in 1810. Cancer and tuberculosis can occur in the same individual and in the same organ.

In 1830 Rokitansky claimed there was a mutual antagonism between cancer and tuberculosis. This doctrine was assailed by the French school under Lebert (1844-51). Experience has proved Lebert's views to have been correct. With the gradual accumulation of pathologic facts we know there is no specific antagonism between cancer and tuberculosis, and that cancer and tuberculosis can occur in the same individual and in the same organ.

A great deal of careful work has been done upon this subject, and the academic discussion that has centred around the question has produced an extensive literature. In Germany some of the more modern articles of worth are those by Lubarsch, Borst, Zenker, Ribbert, Naegeli, Baumgarten, Barchasch, Ehrler, Tauschwitz; in France we have the classic monograph of Claude; in America the articles of Pepper and Edsall, Crowder, Warthin, Moak, Bastedo, Stettin, and Oertel. Bastedo deals with the association of cancer and tuberculosis in general, and gives a summary of the literature. Stettin ably deals with the coexistence of tuberculosis and carcinoma in the intestine. Oertel discusses the relative local influence of coexisting tuberculous inflammation and cancer; he emphasizes the fact that enlarged glands in the neighborhood of a malignant tumor may be tubercular and show no evidence of malignancy. This fact must be kept in mind in weighing the clincial value of enlarged glands in the determination of malignancy (see Table B).

The combination of tuberculosis and carcinoma of the stomach is rare. Case No. 1 was discovered by operation, the remaining cases by autopsy.

The interesting point in this case, beside the association of these two supposedly antagonistic lesions, is the sequence of the lesions.

[1] The case was shown before the Surgical Section of the Academy of Medicine, 1907. The pathologic specimen was demonstrated before the Society of Clinical Surgery, 1907, by Prof. F. C. Wood.

From the clinical and pathologic evidence it seems probable that the original lesion of the stomach was a tuberculous ulcer of the pylorus, secondary to possible old lesion of the right apex. From this tuberculous ulcer a diffuse carcinoma developed.

The following is a summary of the reported cases of combined tuberculosis and cancer of the stomach, and includes a personal case upon which a partial gastrectomy was performed:

TABLE A.—COMBINED TUBERCULOSIS AND CARCINOMA OF STOMACH.

CASE I.—Lyle, H. H. M. (1907). Combined tuberculosis and carcinoma of the stomach; partial gastrectomy; death two years and two months later. Patient, aged forty years. Irish, porter by occupation, admitted May 2, 1907; discharged cured, May 30, 1907.

History: One brother and sister died of pulmonary tuberculosis. Patient had lues sixteen years ago; treatment for two years. Gonorrhea four times. Operated on for fistula in ano four years ago. Drank ten to fifteen whiskies a day; smoked to excess. Has had a "stomach cough" for a year or more. Five months ago he complained of a dull pain in the region of the stomach; this was accompanied by a moderate amount of gaseous distention; the pains and distention have gradually increased. The patient started vomiting four months ago, and this has persisted. The vomiting took place three to four hours after eating; the vomitus was large in amount, and consisted of the contents of the stomach and undigested food; at times it contained food that had been eaten three or four days previously; has vomited coffee-ground material. Constipation marked; bowels have not moved for seven days. Has lost thirty pounds in three months, and has rapidly grown weaker.

Physical Examination: Man, medium frame, emaciated; weight, one hundred pounds. Skin and mucous membranes anemic; superficial glands enlarged. Possible old tuberculous lesion at right apex. Abdomen: Flat, with visible peristalsis; on deep palpation a hard mass about the size of a walnut was found in the epigastric region to the right of the median line; was movable; moved with respiration, and could be fixed with the hand. Lower border of the stomach, two fingers' breadth below the umbilicus, succusion splash was present. Blood: cells normal; hemogoblin, 70 per cent. Gastric analysis: total acidity, 49; HCl, 20; loosely combined, 13; lactic acid present; starch poorly digested; mucus abundant; no blood; no pus; sarcinæ ventriculi and Boas-Oppler bacilli present. A full evening meal was given. The contents expressed next morning contained partly digested meat and raisins. The raisins had been given four days previously.

Diagnosis: Carcinomatous stricture of pylorus, with dilatation of stomach.

Operation by Dr. Lyle, May 5, 1907. Partial gastrectomy, with gastrojejunostomy, according to Billroth's second method. The portion removed included two inches of the duodenum, the pylorus, and the stomach to the Hartmann-Mikulicz line, with the corresponding glands.

Pathologic Report, by Prof. Francis C. Wood. Diffuse carcinoma of the stomach; tuberculosis of submucosa.

Macroscopic Examination: The specimen consists of a complete section of pylorus, plus a portion of the stomach 8 c.m. in length. At the pyloric end the wall is thickened to 1 cm. by dense tissue, which has a uniform light colored, cut surface. Glands enlarged.

Microscopic Examination: Sections show the mucous membrane in places to be entirely gone; the submucosa is infiltrated, with small round cells. The muscular coats have long rows and small groups of gland cells situated between the muscular fibers. The groups of cells are to a marked degree surrounded and infiltrated with numerous small round cells. We also find two or three areas of coagulation necrosis, one of which contains well-formed giant cells and some epithelial cells.

The patient made an uneventful recovery. There was no shock, and the highest temperature was $100\frac{2}{5}°$. He left the hospital May 30, 1907.

Subsequent History: July 2, 1907. Patient has gained forty-five pounds, is working, carrying trunks, etc.; feels well and strong. Eats and digests well. Calmette's ocular test for tuberculosis negative.

September. Has had an attack of diarrhea after partaking of a generous meal of corned beef and cabbage. Attack controlled by the administration of dilute HCl with meals.

February, 1908. Patient continues in good health. Does not react to tuberculin. Has been drinking ten to twelve whiskies a day, without any apparent effect.

March 28. Patient is in good health; no signs of recurrence. Ewald's test meal given. At the end of one hour the stomach was found to be empty. Contents expressed one-half hour after the test-breakfast gave the following results on chemical examination: No free HCl; total acidity, 1.8; no lactic acid; no Boas-Oppler bacilli; no sarcinæ ventriculi; no blood; very little mucus The patient remained well and continued steadily at work for two years and two months. He was admitted to the tubercular service, with the diagnosis of pulmonary tuberculosis, and developed what was supposed to be an acute intestinal obstruction from adhesions. Under local anesthesia an exploratory laparotomy was performed. On opening the abdomen considerable blood-tinged serum escaped. The intestines were equally distended; no mechanical obstruction

was found. The visceral and parietal peritoneum were studded with numerous small tubercles. The condition was paralytic, not mechanical. The distention was relieved by the formation of a left inguinal colostomy. The operation afforded only temporary relief, as the patient died two days later.

Autopsy, by Dr. Zinsser, July 8, 1909. Body of an emaciated man of middle age. On the abdomen to the right of the midline there is a longitudinal incision, extending 2 cm. below the ensiform to the umbilicus. In the left iliac region there is a fresh colostomy wound. Thorax: on opening the thorax, viscera are found in normal position. The anterior mediastinum is obliterated by adhesions of the pericardium. The pericardial cavity is obliterated by adhesions between the pericardium and the heart. Heart: changes of fatty myocarditis. Lungs: both lungs are adherent throughout their pleural surfaces to the thoracic walls, and are thickly studded with tuberculous foci, which in the lower lobes adhere to the miliary type, becoming thicker and individually larger in the upper lobes. Here areas of phthisical consolidation are seen and a few small cavities are found. The bronchial nodes are enlarged and one or two are cheesy. Abdomen: the peritoneum, both visceral and parietal, is studded with miliary tubercles, which are apparently thicker in distribution in the upper quadrant. Liver and spleen show changes of congestion; pancreas apparently normal. Kidney: changes of parenchymatous nephritis; suprarenals, normal. Stomach: at the site of the old operation there is a hard tumor, about 1 x 2 cm. Intestines show no lesions apart from the miliary tubercles on their serous surfaces. Intestinal walls are extremely friable and much discolored, probably due to postmortem conditions. Bladder, normal.

Anatomic Diagnosis: Pulmonary tuberculosis; miliary tuberculosis of peritoneum and of the intestinal coverings; carcinoma of the stomach; parenchymatous nephritis; and fatty degeneration.

Microscopic Examination: Examination of the scar at the site of the gastric operation shows an infiltration of scar tissue, with carcinomatous cells of a type similar to the original growth. Lungs: typical tuberculosis, both miliary and larger phthisical consolidations. Liver: slightly congested, otherwise normal, except for a few small foci, consisting of acute abscesses, not tuberculous.

Case II.—Claude (1899). Alveolar epithelioma and tuberculous ulceration of the stomach. Male, aged sixty-one years. Diagnosis: intestinal and pulmonary tuberculosis; no gastric symptoms. Autopsy: tuberculous lesions of large intestine; tuberculous granulations and caseous softenings of both apices; glands of gastrohepatic omentum and along greater curvature enlarged. On the posterior wall of the stomach near the pylorus is an irregular rounded tumor, 6 cm. by 45 mm., pink in color, covered with villous processes. A short distance from this growth

were other small pedunculated growths about the size of peas. The entire portion of the tumor opposite the pylorus was surrounded by a shallow ulceration; 25 mm. of mucous membrane had disappeared from the base of the ulcer.

Microscopic examination shows the growth to be an alveolar epithelioma, with cylindric or polymorphous cells, forming a voluminous tumor, which has been invaded by tuberculosis and in part destroyed by this superadded infection. The small pea-like growths were adenoma. Section through the ulcer showed giant cells, containing tubercle bacilli. Claude was of the opinion that cancer developed on the basis of an adenoma, and that the tuberculosis was superadded.

CASE III.—Simmonds (1900). Carcinoma of the plyorus, with multiple tuberculosis ulcers. Man, aged forty years, died of pulmonary and intestinal tuberculosis. At autopsy a coarse carcinoma the size of a hazel-nut was found, which caused stenosis of the pylorus. The distended stomach contained several small tuberculous ulcers. The observer suggests that the secretory disturbance due to the presence of the carcinoma and diminished production of hydrochloric acid served to favor the growth of the tubercle bacilli in the gastric mucosa.

CASE IV.—Barchasch (1907). Submucous tubercle of the pylorus, with simultaneous carcinoma of the cardia.

Autopsy: the subject, aged forty-five years, presented the following findings, with a simultaneous carcinoma of the cardia orifice; carcinoma of the regional glands; old pulmonary tuberculosis. The rare form of gastric tuberculosis, in the shape of a solitary tubercle, gave no clinical evidence of its presence during life, and was not discovered until autopsy. The interest in this case consists in the combination of tuberculosis and cancer in the stomach. The origin of tuberculosis of the stomach was considered secondary to the pulmonary process, the lack of the HCl favoring the development of the tubercle bacilli.

Microscopic Examination: Adenocarcinoma tuberculosis. Tubercle bacilli were found in the sections of the tubercle. Glands, adenocarcinoma.

CASE V.—Borst. Carcinoma of stomach, with multiple tuberculous ulcers. No clinical details given; case of phthisis, with multiple tuberculous ulcers and carcinoma of the stomach. The stroma of the carcinoma contained tubercle bacilli. Borst considers this a carcinoma invaded by tuberculosis.

CASE VI.—Friedländer. Cancer of the stomach developing on a cicatrix of a round ulcer, which had been invaded by tuberculosis. This case is quoted by Claude (p. 60). I have been unable to verify it.

TABLE B.—ABSTRACT OF CASES WITH CARCINOMA OF THE STOMACH ASSOCIATED WITH TUBERCULOUS LYMPHATIC GLANDS.

Clement (1895). Pyloric carcinoma associated with extensive caseous tuberculosis of the pyloric glands, the glands of the hilum of the liver, and axillary glands.

Metterhauser (1897). Carcinoma of the pylorus, miliary tuberculosis of the liver, and the mesenteric lymph glands.

Naegeli (1897). Carcinoma of the pylorus; caseous tuberculosis of the regional glands.

Lowenstein, quoted by Tauschwitz (p. 17). Have been unable to find original.

Ehrler (1906). Adenocarcinoma of the pylorus, with tuberculosis of retroperitoneal glands. Pylorectomy with gastro-enterostomy, peritoneal infection from leakage, tuberculosis of the rectoperitoneal glands, intestinal tuberculosis, phthsis.

The cases of Archard and Kollech are not included in this table.

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THE CONTROL OF RABIES.[1]

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Historical Note. Although reference is made to a disease in dogs, which was no doubt rabies, by Aristotle, as long ago as the fourth century before the Christian era, and distinct epidemics of the disease were recognized as far back as the beginning of the seventeenth century, it was not until about 1875 that it was demonstrated that the disease could be markedly limited in its spread and probably entirely stamped out. Accordingly at about that time several nations adopted rigid regulations for the control of the disease. Such nations have been abundantly rewarded; the disease no longer existing in Great Britain, Norway, Sweden, nor Denmark. With such a remarkable demonstration of the efficacy of a preventive measure it seems indeed strange that most of our civilized nations have not yet adopted measures which if carried out may be relied upon to exterminate the disease. This in face

[1] Read at the Fifteenth International Congress on Hygiene and Demography, Washington, D. C., September, 1912.

of the fact that, taken the world over, the disease is apparently on the increase.

PREVALENCE OF RABIES IN THE WORLD AT THE PRESENT TIME. Rabies is a very widespread disease. With the exception of Australia there is not a continent which is free from it. It is apparently most prevalent in the countries of Europe adjacent to the Mediterranean Sea. On account of the fact that in most countries the disease is not reportable, except as it causes the death of a person, it is impossible to obtain even fairly accurate data as to the number of cases of rabies now in existence. The figures presented in the following table give therefore only an approximate idea as to the number of persons who are annually bitten by rabid or presumably rabid animals:

NUMBER OF PERSONS BITTEN BY RABID OR PRESUMABLY RABID ANIMALS IN VARIOUS COUNTRIES.

Country.	Number.	Year.	As determined by the number of persons who received the Pasteur antirabic treatment at:
Argentina	417	Average of past twenty-four years	Buenos Aires.
Australia	...[2]		
Austria	452	Average of 1907 and 1908	Vienna.
Brazil	583	1911	Sao Paulo
Bulgaria	1027	1911	
Canada	...[3]		
Denmark	0	For past fifty years	
France	467	1909	Paris.
Germany	374	1909	Berlin and Breslau.
Great Britain	0	Since 1902	
Hungary	806	Average 1890 to 1908	Budapest.
Holland	...[4]	Since 1879, except along the Belgian border	
India	2073	1910	Kasauli.
Italy	3537	1909	Rome, Milan, and Turin.
Philippine Islands	54	Year ending June 30, 1911	Manila.
Portugal	1672	1911	Lisbon.
Russia	3520	1909	St. Petersburg and Charkaw.
Spain	649	1911	Madrid and other places.
Sweden	0	Since 1870	
Switzerland	0	1911	
Turkey	978	1908	Constantinople.
United States	4625	1911	

PREVALENCE OF RABIES IN THE UNITED STATES. In 1900, Salmon[5] reported that there had been 230 deaths of human beings from rabies in 73 of the principal cities of the United States, from 1890 to 1899.

According to the mortality statistics of the Bureau of the Census the number of deaths of human beings from rabies in the registration area of the United States was 33 in 1900, the number gradually increasing to 85 in 1906, and falling to 75 in 1907.

The Public Health and Marine Hospital Service made an exhaustive study[6] into the prevalence of the disease in the United States in 1908. According to their findings, rabies was present in

[2] Never introduced. [3] Never introduced. [4] Few cases.

[5] Salmon, D. E. Year-book, Dept. Agri., 1900.

[6] Kerr and Stimson. Jour. Amer. Med. Assoc., September 25, 1909, liii, 989.

534 localities distributed throughout the United States, with the exception of 10 States; there occurred 111 deaths of human beings and about 1500 persons received the Pasteur antirabic treatment.

During the past few months I have collected the data relative to the prevalence of the disease in the United States during the year 1911. Data were also collected by the Public Health and Marine Hospital Service.[7] Such data have been combined in the form of the following table:

States.	Infected localities.		Persons treated in	Disease on increase or decrease—determined by comparing number of cases of the disease in 1911 with those of the previous three years.			Possess State regulation for the control of rabies in dog.
	1908	1911	1911	Increase.	Decrease.	Uncertain.	
Alabama	13	47	281	*			
Arizona	1	1	1	..	*	..	*
Arkansas	5	18	29	*			
California	..	49	124	*			
Colorado	1	10	10	*			
Connecticut	7	11	8	..	..		
Delaware	5	15	22	*			
District of Columbia	1	1	41				
Florida	11	36	128	*			
Georgia	17	4	457	*			
Idaho							
Illinois	18	35	292	*			
Indiana	57	62	104	*			
Iowa	5	29	92	*			
Kansas	4	86	175	*			
Kentucky	7	14	24	*			
Louisiana	3	61	233	*			
Maine							
Maryland	12	59	122	..	..	?	
Massachusetts	9	45	27	..	*		
Michigan	11	46	58	*			
Minnesota	18	31	117	..	..	?	
Mississippi	10	34	51	*			
Missouri	9	52	187	*			
Montana							
Nebraska	5	..	..	..	..	?	
Nevada							
New Hampshire	7	3	2	..	*		
New Jersey	41	68	189	*			
New York	52	38	899	..	*	..	*
New Mexico							
North Carolina	19	96	166	*			
North Dakota	2	12	15	*			
Ohio	32	91	275	*			
Oklahoma	6	51	106	*			
Oregon	..	3	1	..	*		
Pennsylvania	25	52	46	..	*	..	*
Rhode Island	10	4	5	*			
South Carolina	5	32	114	*			
South Dakota	2	7	14	..	..	?	
Tennessee	7	16	13	*			
Texas	15	..	..	..	..	?	
Utah							
Vermont	1	..	0	..	*	..	*
Virginia	37	48	54	..	..	?	
Washington	..	7	2	*			
West Virginia	2	21	30	*			
Wisconsin	42	83	112	..	..	?	
Wyoming	..	3	4	*			
Total	534	1381	4625	27	7	7	4

[7] Stimson, Public Health Reports, July 12, 1912, vol. xxvii, No. 28.

A comparison of the distribution of rabies in the United States in 1908 and 1911 indicates that during the last three years:

1. There has been an increase of rabies in the United States, as indicated by the fact that during 1908 there were 534 infected localities and about 1500 persons received the Pasteur antirabic treatment, whereas in 1911 there were 1381 infected localities and 4625 persons received the treatment.

2. The increase has occurred principally in the Southern and Middle Western States, very few of which have any State regulations concerning the muzzling and movement of dogs.

3. There has been a decrease in the number of cases in most of the New England States, where since the epidemic of rabies several years ago regulations aiming at the control of the disease in dogs have been rather rigidly enforced. In Rhode Island the relaxation in the enforcement of muzzling regulations during the past two years is causing a distinct increase in the number of cases.

4. The disease is somewhat on the increase in the far west, more especially in California. It is believed by some that the spread of rabies in Arizona is due principally to the bite of skunks. With the object of controlling the disease a bounty is being paid for skunks in that State. The secretary of the State Board of Health of Montana informed me that so far as known there has never been a case of rabies within its borders. It would be unfortunate if the disease should gain a foothold among the wild animals of the west, as it has done in some countries.

It is well understood that infection with rabies takes place almost only through a wound, such as the bite of an animal, and that, although any of the warm-blooded animals may be affected, the dog is by far the principal offender.

Methods Which May be Employed for the Control or Eradication of Rabies. *Immediate Local Treatment.* The development of the disease can be largely prevented by treatment of the wound with some caustic, preferably nitric acid. Cauterization should, of course, be done as soon as possible after the wound is inflicted. Experiments performed in the research laboratory of the New York City Department of Health indicate that the application of nitric acid is of value even if such application be delayed for twenty-four hours. Dr. Park believes that "in the case of small wounds all the treatment probably indicated will be thorough cauterization with nitric acid within twelve hours from the time of infection."

Pasteur Antirabic Treatment. The Pasteur treatment has largely robbed rabies of its terrors. Previous to 1886, when the treatment was first begun at the Pasteur Institute in Paris, the mortality from rabies of persons bitten by rabid or presumably rabid animals was 16 per cent. (Leblanc). Since that time more

than 30,000 persons have received the preventive treatment at the Paris Institute, with a mortality of only 0.5 of 1 per cent. The Pasteur treatment is given in most of the countries of the globe, and through the Public Health Service is made available in every State of the United States. The results at other institutes have been practically the same as those of the institute at Paris. However efficient this treatment has been in preventing the development of the disease in infected individuals it is probable that the safety assured by the treatment has caused a relaxation in the enforcement of regulations aiming at the control of the disease in dogs and other lower animals. Dr. T. Murillo recently informed me that he believes that for the reason mentioned there are more cases of rabies in Spain at the present time than there were twenty years ago.

Accurate Diagnosis. In practically all countries the clinical diagnosis is confirmed whenever possible by a laboratory examination, consisting of a search for Negri bodies or of an animal inoculation, or both. The mistake that is often made is the killing of the animal so soon as rabies is suspected. If the animals are detained and watched for the development of the disease instead of being killed it will be found that some of the Pasteur treatment which is now being given is unnecessary, but at the present time advisedly administered.

Regulations Aiming at the Control of Rabies in Dogs and Other Lower Animals. Although rabies may be transmitted by the bite of any of the warm-blooded animals the disease is propagated principally by dogs. For that reason regulations aiming at the eradication of the disease, with but occasional exceptions, must be aimed at dogs. The enforcement of the following measures may be relied upon to cause the extermination of rabies:

Licensing. Stray ownerless dogs are the principal offenders, not only in spreading rabies, but in doing harm to live stock. Irrespective of the presence of rabies in a community all dogs ought to be licensed and provided with a collar and license tax and all stray dogs destroyed in a humane manner. The expense of enforcing such a license rule may be maintained by the dog-license fees. The rule has been enforced in England and in the other countries from which rabies has been eradicated. The present decline of the disease in Paris is attributed by Dr. Letulle to the strict enforcement of the regulations regarding the capture of stray dogs.

Muzzling. Wherever rabies is present in a given place all dogs permitted to run at large should be kept muzzled for a period of at least six months after the disappearance of the last case from the locality. There is a difference of opinion as to the size of the territory in which dogs should be muzzled whenever the disease appears. Certainly it should not be less than a city of moderate

size, or in rural communities it should in the United States not be less than an average-sized township. If several cases occur at places several miles apart it is advisable to have the regulations enforced over an area corresponding to a county. If the disease is widespread it is certainly best to have the dogs of an entire State muzzled. The muzzling of dogs is the most important measure in preventing the spread of rabies in a community where the disease exists. In the larger cities of Germany dogs permitted to run at large are always muzzled. The objection to muzzling comes from many well-meaning people who believe that it is cruel. It is not cruel to place a properly constructed (such as the basket type, made of metal) and well-fitting muzzle on a dog. Such a muzzle will permit the dog to open its mouth, pant, and drink, but not to bite. It is no more cruel to put a muzzle on a dog than a bit in a horse's mouth. Of course the dog will resent it at first; so does the horse resent the bit. But once they become accustomed to it they do not mind it. The good effect of this procedure has been demonstrated many times and in many places. Probably the best example is the result brought about in England, as is well shown by the following table:

NUMBER OF CASES OF RABIES IN GREAT BRITAIN.

Year.	Number of cases.	
	Dog.	Human.
1887	217	29
1888	160	14
1889	312	30
Muzzling enforced:		
1890	129	8
1891	79	7
1892	38	6
Opposition to muzzling; ordinance relaxed:		
1893	93	4
1894	248	13
1895	672	20
Muzzling again enforced:		
1896	438	8
1897	151	6
1898	17	2
1899	9	0
1900	6	0
1901	1	0
1902	13	0
1903–07	0	0

Note that with the enforcement of the muzzling law the number of cases of rabies rapidly declined from 217 in 1887 to 38 in 1892. In 1892 the authorities yielded to the petition of "dog lovers" and permitted muzzling to be discontinued. As a result the disease rapidly increased in number, so rapidly that during the third year (1895) 672 dogs and 20 human beings died from rabies. The

muzzling law was again enforced, the number of cases rapidly decreased, and in 1902 entirely disappeared. Since that time no case of rabies has been recognized in Great Britain. Dogs are not muzzled in England at the present time, but we are informed that muzzling will be resumed with the appearance of a single new case of the disease. The existence of a muzzling act should require all dogs not muzzled to be killed by the proper health or police authorities. In some places the right to kill any unmuzzled dog is given to any person. If the law held the owner of a dog legally responsible for all damage done by such, muzzling could be enforced much more readily than is the case at present.

Detention of Dogs. Dogs that have been associated with rabid animals, and are therefore probably infected, should be confined to a kennel or shed for a period of not less than three months, and preferably six months. When taken out for exercise they should be muzzled and led in leash. When the disease is prevalent it is best to have all dogs confined. Females in heat should at no time be permitted to run at large.

Destruction of Dogs. All dogs known to be affected by rabies or to have been bitten by rabid animals should be killed. The mistake that is usually made is to kill an animal immediately after that animal has bitten a person, on the suspicion that it may be affected by rabies. The importance of such an error is realized when we remember that it is not always possible to get laboratory evidence of the disease even when it exists. Whenever possible an animal that has bitten a person should be kept confined for a period of ten days. If the disease does not develop nor the animal die within that time it may be safely concluded that rabies does not exist.

Quarantine. To prevent the introduction of rabies into a country, all dogs that are imported should be held in quarantine for a period of six months. Australia owes to a rigid enforcement of such a law the fact that it has never had a case of rabies. England likewise depends on it to keep the country free from the disease. Such quarantine may likewise be applied to the smaller divisions of a country. During a recent outbreak of the disease in Canada it was prohibited to move dogs from the infested area. In Germany a certificate from an official veterinarian is necessary to have a dog moved from one section to another. The Federal Government might impose a quarantine against a given State should the disease become prevalent within its borders.

There are few diseases that can be so easily eradicated as rabies. We have now the knowledge necessary to secure its disappearance. All that we need is action on the part of our authorities, which to be effectual must of course have the coöperation of the general public. The time is now ripe for organized effort to stamp out

the disease. It has been done in England and can likewise be done in other insular territories. It has been accomplished in Norway, Sweden, and Denmark, and can likewise be done in other peninsular regions. It is more difficult to rid of rabies, inland countries with extensive land boundaries. Even in these much can be accomplished, as has been demonstrated by Germany, Holland, Canada, and some of the eastern States of the United States. It is hardly to be expected, however, that the disease will be entirely eradicated without coöperative or at least simultaneous action on the part of adjoining States or countries. In the United States the question of State rights requires that the efforts be left largely with the individual States. If every State in which the disease exists would take as vigorous steps to exterminate rabies as were taken in England, and if like action were taken by the countries to the south of us, as has substantially already been done by Canada on the north, it would be possible to remove the last vestige of the disease from the North American continent in the course of a few years. In like manner the disease could be eradicated from other continents.

To exterminate rabies it is necessary that the general public should be better informed than it is at present regarding the disease. The people should be made to realize especially:

That rabies is prevalent in most countries the world over, and that in many places—more especially in parts of the United States—it is distinctly on the increase.

That it is possible to exterminate the disease in the course of a few years by the adoption of easily executed regulations concerning dogs.

That in particular the muzzling of dogs is not a hardship to the animal, and that from a sanitary and economic point of view it is advisable to get rid of all stray or ownerless dogs.

That the eradication of rabies is worth while for economic reasons because of the loss to the live-stock industry.

That efforts at its eradication are many times over justified by the loss of human life and the almost endless amount of worry which is now attached to the bite of a dog.

METABOLISM IN PELLAGRA.[1]

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Introduction. A study of the metabolism in pellagra would appear to be of interest from a number of different viewpoints—namely, as an aid to the interpretation of the gastro-intestinal symptoms generally observed; in connection with the maize theory of the etiology of the disease; and, further, because of the resemblance in certain particulars to beriberi,[2] in which the etiologic factor appears to be an inadequate dietary. Despite the reasons which would seem to make a knowledge of the metabolism in this disease desirable no extended study has been carried out in this connection, with the exception of the work of Camurri,[3] in Italy. However, certain points of interest have been noted—namely, the frequent occurrence of gastric anacidity by Johnson,[4] by Cecconi,[5] and by Niles,[6] and the presence of indicanuria by a number of observers, most recently by Ormsby and Singer.[7]

The experiments conducted by Camurri were fairly comprehensive, though directed in particular toward the study of the mineral metabolism. His work included a general study of the composition of the diet, urine, and feces of pellagrins subsisting upon mixed diets and upon diets composed largely of corn. Balances were given for nitrogen, fat, and salt in comparison with

[1] This paper forms a part of the preliminary report of work performed under the auspices of the Thompson-McFadden Pellagra Commission of the Division of Tropical Medicine, Department of Laboratories, New York Post-Graduate Medical School and Hospital. The results of this work were reported at the Second Triennial Meeting of the National Association for the Study of Pellagra, Columbia, S. C., October 3, 1912, and at a meeting of the Section on Medicine of the New York Academy of Medicine, February 18, 1913. The analytical work was carried out with the assistance of Messrs. G. O. Volovic, W. I. Sivitz, Dr. E. Kister, and Mr. A. Bernhard; and the ward work with the assistance of Mrs. J. H. Brinkerhoff and the Misses H. A. Macarow and H. F. McDowell.

[2] For discussion of literature on beriberi, see Strong and Crowell, Philippine Jour. Sci., 1912, B, vii, 271.

[3] Atti del Quarto Congresso Pellagrologico Italiano, Udine, 1910, p. 67.

[4] South. Med. Jour., 1911, iv, 478.

[5] Gazzetta Degli Ospedali e delle Cliniche, 1911, xxxii, 77.

[6] Pellagra, 1912, p. 77.

[7] Report of the Pellagra Commission of the State of Illinois, 1911, p. 23; also Arch. Int. Med., 1912, x, 123 and 219.

those of normal individuals upon similar diets. The points of interest will be discussed in connection with our own work.

Johnson found the free hydrochloric acid of the gastric juice to be absent in 14 out of 20 cases, while rennin was absent in 7 cases. Diarrhea was observed in the 14 cases, with absence of free hydrochloric acid, but only in one of the other 6 cases, and here attributed to another cause. Cecconi found free hydrochloric acid absent in all of his 12 cases, while Niles in an examination of 64 cases of undoubted pellagra found free hydrochloric acid absent in 18, deficient in 31, excessive in 12, and normal in 3. He noted that the gastric secretions were diminished or absent in most cases of long standing, while in the few instances where those juices were increased the cases were acute.

In a study of 55 cases of pellagra, Tucker[8] reported an increase in indican in 3 cases. In the report of the Illinois Pellagra Commission, however, Ormsby and Singer noted a marked reaction for indican in all the cases examined.

The experiments here reported were made upon the patients sent to the Post-Graduate Hospital by the Thompson-McFadden Pellagra Commission. We have endeavored to make a fairly extensive study of the metabolism in pellagra, because a thorough knowledge of the fundamental processes of metabolism appeared particularly desirable in this disease; and, further, because it was believed that points of attack might be disclosed which would offer opportunities for more intensive study.

Methods Employed. The general procedures employed in this metabolism study were to secure gastric contents (after the Ewald-Boas meal) as soon as practical after the admission of the patient to the hospital. Subsequently the patient was placed upon a weighed diet, and the urine and feces collected daily for a period varying usually from seven to ten days. Following this period, gastric contents were again secured in certain of the cases, while in two instances a second metabolism experiment was conducted.

The examination of the gastric contents has been directed particularly to determining the acidities and ascertaining the peptic activity. The customary titration methods were employed for the acidities and Rose's method for pepsin, as conducted in this laboratory.[9]

During the period of the metabolism study a lacto-vegetarian and practically purin-free diet was employed for experimental reasons. The general type of the diet may best be illustrated by a sample day (August 8) taken from Case VIII (M. T.).

[8] Jour. Amer. Med. Assoc., 1911, lvi, 246.
[9] Post-Graduate, 1912, xxvii, 506.

	Grams or c.c.
Breakfast:	
Corn-flakes	25
Banana	89
Bread	63
Egg	48
10.30 A.M.	
Water	150
Apple	105
Dinner:	
Apples	125
Water	50
Bread	127
Egg	43
Potato	140
3.00 P.M.	
Graham crackers	26
Supper:	
Cream of wheat	25
Water	300
Bread	101
Egg	46
Orange	148
Water	200
10.00 P.M.	
Banana	97
Distributed between the various meals as desired:	
Cane sugar	63
Milk	800
Butter (salt free)	23
Salt (pure NaCl)	6

This would furnish 91 grams protein (14.6 N × 6.25), 71 grams fat, 460 grams carbohydrate and would yield approximately 2800 calories, which is not far from the average found for the period in this case.

As insufficient time prevented our making a complete analysis of the food intake, the figures for protein, carbohydrate, and fat were for the most part calculated from the data given by Atwater and Bryant[10] for American food materials, while the figures for the mineral constituents were taken from results compiled by Sherman.[11] Many of the figures for nitrogen, however, were from our own analyses, and we believe that the results which we have given for the nitrogen intake are reliable. The protein intake has been calculated from the nitrogen figures by employing the factor 6.25, and the calorific intake obtained by multiplying the grams of protein and carbohydrate by 4 and the grams of fat by 9 and adding these results.

[10] United States Dept. Agri., Office of Exper. Sta., Bulletin 28, Revised, 1906.
[11] Chemistry of Food and Nutrition, 1911, p. 332.

Previous to beginning the metabolism study the patients were placed for several days upon the diet they were to receive during the period of actual examination. The end of the twenty-four-hour urine period was taken as 7.30 A.M. After the excretion of the last sample of urine for the day the patients were weighed and then given their breakfast. The urine specimens were collected in three-liter glass-stoppered bottles and preserved with a liberal supply of toluene. The urines were taken to the laboratory at 9 A.M., made up to some definite volume (1000 c.c. where possible), and the nitrogenous constituents, the ammonia in particular, determined in most cases the same day. At this time the qualitative and microscopic examinations were made. The urines were then refrigerated at 0° C. for future use. The feces were collected in weighed tin pails, the weight of the feces ascertained by difference, and then kept in a common receptacle in the refrigerator at —4° C. until the end of the period. In most of the experiments the feces of the experimental period were marked off with charcoal, though in some of the later experiments carmin was employed. When the feces for the whole period had been assembled, they were thoroughly mixed and a weighed portion, generally one-half, dried over the water-bath with the addition of alcohol acidified with dilute sulphuric acid, and subsequently ground to a fine powder. All determinations with the exception of the indol and skatol were made upon the air-dried feces.

The examination of the urine included the usual qualitative tests—namely, tests for albumin, sugar, acetone diacetic acid, and a microscopic examination of the centrifugalized sediment, and, in addition, quantitative estimations of the total nitrogen, urea, ammonia, uric acid, creatinin, creatin, chlorides, phosphates, inorganic and ethereal sulphates, neutral sulphur, total acidity, and indican on the individual specimens, and determinations of sodium, potassium, calcium, and magnesium on composite samples. The methods employed were: For total nitrogen, Kjeldahl; for urea, the Benedict (S. R.) method;[12] for ammonia, uric acid and creatinin, the Folin methods;[13] for creatin, the Benedict (F. G.)-Myers' modification of the Folin method;[14] for chlorides, the Volhard-Arnold method; for phosphates, uranium nitrate; for inorganic and ethereal sulphates, the Folin methods;[15] for neutral (total) sulphur, Benedict's (S. R.) method;[16] for total acidity, Folin's method; indican as described by Myers and Fine;[17] the sodium and potassium in part as directed by Folin,[18] the potassium

[12] Jour. Biol. Chem., 1910, viii, 405.
[13] Amer. Jour. Phys., 1905, xiii, 45.
[14] Ibid., 1907, xviii, 397.
[15] Jour. Biol. Chem., 1905-6, i, 131.
[16] Ibid., 1909, vi, 363.
[17] Post-Graduate, 1912, xxvii, 1144.
[18] Handbuch der Biochemichen Arbeitsmethoden, 1911, v, Pt. I, 292.

being estimated by the Drushel cobaltinitrite[19] method, and calcium and magnesium as described by McCrudden,[20] the calcium being estimated volumetrically.

The examination of the feces included certain of the simple routine tests and, in addition, estimation of moisture, nitrogen, fat, carbohydrate, mineral constituents, and the putrefactive products, indol and skatol. The moisture was obtained from the difference in the weight of the moist and air-dried feces. The nitrogen in the air-dried feces was estimated by the Kjeldahl method, the fat on the thoroughly dried feces by the Soxhlet method with anhydrous ether, and the carbohydrate with the Allihn method after hydrolysis of the feces as described by Mendel and Fine.[21] The mineral constituents were estimated in a similar manner to that described for urine. The indol and skatol were determined upon samples of the moist feces, with the aid of Ehrlich's aldehyde.[22] The feces slightly acidified with sulphuric acid were subjected to steam distillation until they failed to give a reaction with this reagent. A portion of the distillate was treated with the reagent to the maximum color, extracted with chloroform, and matched up in a Duboscq colorimeter with a similar extract prepared from mixtures of pure indol and skatol, showing the same color as the specimen under examination. It is believed that in this way an approximation of the amounts of both indol and skatol present was obtained.

Case Histories. A brief history of the cases upon which this study was made follows. A more detailed consideration of the case histories will be taken up in a subsequent paper of this series.

Case 1.—J. A. (Pellagra Commission, No. 1, Union County). Fairly well nourished man, aged sixty years; lesions rather slight; some scaling on hands; no evidence of diarrhea.

Case 2.—M. F. (Pellagra Commission, No. 1, Spartanburg County). Thin, pale, rather poorly nourished girl, aged seventeen years; no marked lesions; had had ovariotomy; no evidence of diarrhea.

Case 3.—M. McH. (Pellagra Commission, No. 2, Spartanburg County). Fairly well nourished woman, aged thirty-seven years; marked erythema on backs of hands and wrists; some erythema on face and mouth; developed acute mania while in hospital; strangyloides intestinalis observed; moderate diarrhea.

Case 4.—C. T. (Pellagra Commission, No. 12, Spartanburg County). Well-nourished woman, aged forty years; very slight scaling on hands; not sufficiently definite for diagnosis; showed marked improvement.

[19] Amer. Jour. Sci., 1908, xxvi, 555; also Myers, Jour. Biol. Chem., 1909, vi, 115.
[20] Jour. Biol. Chem., 1909–10, vii, 83; 1911–12, x, 187.
[21] Ibid., 1911, x, 339.
[22] Herter and Foster, Jour. Biol. Chem., 1906, ii, 267.

CASE 5.—R. N. (Pellagra Commission, No. 9, Spartanburg County). Moderately well-nourished woman, aged thirty-two years; some scaling on forearms; had had erythema before coming to hospital; recovered while in hospital.

CASE 6.—M. L. (Pellagra Commission, No. 68, Spartanburg County). Tall, thin, poorly nourished woman, aged thirty-six years; said to have had tuberculosis, but no evidence of this could be found while patient was in hospital; some erythema and desquamation on back of hands; condition cleared up quickly.

CASE 7.—E. C. (Pellagra Commission, No. 113, Spartanburg County). Well-nourished girl, aged twenty-years; marked thickening of palms of hands; extensive desquamation on back of hands, forearms, elbows, dorsal surfaces of feet, on and around knees; irregular girdle of desquamation about waist; erythema not evident; case recovered very quickly.

CASE 8.— M. T. (Pellagra Commission, No. 114, Spartanburg County). Fairly well-nourished girl, aged about eighteen years; little erythema and desquamation on backs of hands and forearms; recovered quickly.

CASE 9.—L. G. (Pellagra Commission, No. 115, Spartanburg County). Tall, thin, poorly nourished woman, aged twenty-eight years; scaling on forearms and backs of hands, also slightly in front of neck; dull mentally, although said to have been bright previous to attack.

CASE 10.—M. S. (Pellagra Commission, No. 21, Spartanburg County). Rather tall, thin, poorly nourished woman, aged twenty-eight years; extensive lesions on backs of hands, forearms, arms, shoulders; girdle of erythema around neck; had ovarian cyst.

CASE 11.—B. B. (Pellagra Commission, No. 158, Spartanburg County). Fairly well nourished woman, aged thirty-three years; slight erythema, desquamation and pigmentation on backs of wrists; lesions did not cover great area; had pulmonary tuberculosis as demonstrated by an examination of sputum.

CASE 12.—A. N. (Pellagra Commission, No. 206, Spartanburg County). Fairly well-nourished woman, aged forty-three years; erythema, pigmentation, and desquamation up to middle of back of forearms.

CASE 13.—C. McC. (Pellagra Commission, No. 170, Spartanburg County). Poorly nourished woman, aged thirty-five years; extensive desquamation and discoloration of skin on backs of hands, forearms, arms, shoulders, and around neck; palms of hands much thickened, also deep fissures at points of fingers; marked diarrhea; mentality evidently low; delusions and hallucinations; recovered.

CASE 14.—W. L. (Pellagra Commission. No. 166, Spartanburg County). Fairly well nourished woman, aged thirty-five years;

mild desquamation on forearms. In this case no complete metabolism study was conducted, though an analysis of a twenty-four hour urine, gastric contents, and a qualitative examination of feces were made.

Gastric Analysis. The gastric analyses have shown very interesting results, especially when considered in connection with the indican estimations of the urine. In 8 of the 14 cases free hydrochloric acid was absent. The total acidities were low, and pepsin was generally absent, or present only in small quantity. Though considerable amounts of indican were observed in all cases, the quantity was excessive in those with anacidity, reaching in one case nearly a quarter of a gram a day. To emphasize this relationship the data given in Table I have been arranged in order of the amounts of the average daily indican elimination. This association of high indican elimination, with diminished acidity, is indicative of the strong inhibitory influence of the normally acid gastric juice upon putrefaction in the alimentary canal, or at least a certain type of putrefaction. As may be observed, some of the cases with low indicanuria and with free hydrochloric acid present in the gastric juice have a fairly high elimination of ethereal sulphates, but, in general, the total ethereal sulphates as well as the indoxyl-potassium-sulphate are increased in anacidity. Still another factor which may play a part is the activity of the pepsin, especially in the cases where hydrochloric acid is present. Case 12 (A. N.), with only a slightly subnormal acidity, but with a low peptic activity, showed an elimination of indican next in amount to the cases with anachlorhydria. In this series of cases, anacidity was found in about the same percentage of cases as reported by Johnson. Cecconi in the 12 cases which he examined made qualitative tests for indican. Though all of his cases showed an absence of free hydrochloric acid, no uniform relation appeared to exist between the anacidity and the indican, if we are to accept the qualitative tests for indican as representative of the quantitative elimination.

Food Intakes. In general the food intakes may be viewed as indicating the general condition of the patients, since they were allowed considerable liberty in the choice of food, and further provided with all they desired. The food intakes, as shown in Table III, amounted in all cases to from 75 to 110 grams of protein (12 to 18 grams of nitrogen) and 2300 to 3000 calories per day, with the exception of Case 2 (M. F.), during the first period of observation, and Case 3 (M. McH.) during both periods of observation. With the same exceptions all the cases showed a decided plus nitrogen balance during the period of observation, the degree of nitrogen retention being in proportion in general to the gain in weight as shown in the tabulated results. Case 2 (M. F.) during

the first period of nine days, with an intake of 8.9 grams of nitrogen, showed a slight plus daily balance of 0.6 gram, though a decided plus balance was observed with the gain in weight during the second period. Case 3 (M. McH.), with a nitrogen intake of 5.0 grams during the first period, showed a minus daily balance of 1.4 grams, with a decided loss in weight. During the second period, with a nitrogen intake of 7.2 grams, she gained slightly in weight and showed a plus daily balance of 1 gram nitrogen. Corn in the form of corn-flakes was consumed in all the experiments, while case 2 (M. F.) ate considerable quantities of corn-bread during the second period of observation. During this period of seven days she gained four pounds in weight, showed an average daily nitrogen balance of plus 4.1 grams, and otherwise showed general improvement.

TABLE I.—Gastric Analyses in Comparison with Certain Data of Urine and Feces. Tabulated in Order of Indican Elimination.

Patient.	Gastric analyses.					Urine.			Feces.	
	Volume of contents.	Free HCl.	Total acidity.	Lactic acid.	Peptic content[23] (Rose.)	Indican. Daily average.	Ethereal sulphates as SO_3 Daily average.	Ratio ethereal to inorganic SO_3.	Indol. Daily average.	Skatol. Daily average.
	C.c.					Mg.	Mg.		Mg.	Mg.
13—C. McC.	270	0	5	+	0.5	240	181	1 to 8	—	—
4—C. T.	90	0	8	+	0	208	194	1 to 7	5	10
	180	0	7	+	0					
	50	0	6	+	0					
1—J. A.	94	0	4	+	0	151	207	1 to 6	0	28
	130	0	4	++						
2—M. F.	135	0	14	+	0	128	126	1 to 8	0	2
	60	0	12	+	0	48	98	1 to 11	3	3
9—L. G.	70	0	12	++	0	95	203	1 to 6	11	34
	200	0	4		1					
3—M. McH.	188	0	7	+	2	69	97	1 to 7	2	9
	3	0	—		—	91	122	1 to 5	7	7
	140	0	20	++	7					
8—M. T.	140	0	8	++	0	88	161	1 to 11	3	12
11—B. B.	300	0	4	+	2	71	126	1 to 11	21	51
12—A. N.	65	18	43	..	0.5	65	124	1 to 17	Tr.	Tr.
	20	36	60	..	0.5					
14—W. L.	90	40	64	..	7	57	..	..	—	—
6—M. L.	135	15	32	+	7	45	149	1 to 11	0	1
5—R. N.	35	22	42	..	5	43	59	1 to 20	14	0
	270	14	38	..	10					
	45	26	54	+	7					
10—M. S.	170	8	26	..	16	23	117	1 to 11	2	19
	57	2	20	+	2					
7—E. C.	340	17	34	+	2	21	147	1 to 8	0	16

As the tabulated data show the food intake, with the few exceptions mentioned, was generally up to the standard set by Atwater, and thus far above the minimum figures given by Chittenden. Both the protein and the calorific intake appear to have been

[23] Normally the peptic activity of the gastric juice after the Ewald meal is 8 to 11 by the Rose method.

ample as judged by these standards, though perhaps the proportion of fat to carbohydrate is a little higher than ordinarily found.

These data hardly allow of comparison with the results observed by Wussow and Grindley[24] at the Peoria State Hospital, for the reason that, with one exception, they were all women and, further, were below the normal average weight. At Peoria they found the general diet supplied per man per day: Protein, 73.5 grams; carbohydrate, 444 grams; fat, 56 grams; energy, 2568 calories; mineral matter, 23.23 grams, of which 1.07 grams were phosphorus; while the corn diet gave protein, 87.2 grams; carbohydrate, 463 grams; fat, 79 grams; energy, 2898 calories; total mineral matter, 27.91 grams, of which 1.64 grams were phosphorus. In general the diet of our patients appeared to furnish a somewhat larger amount of protein and fat, but a smaller amount of carbohydrate. The diets employed by Camurri are likewise of interest in this connection. His mixed diet contained 131 grams protein, 430 grams carbohydrate, 66 grams fat, 24.85 grams mineral matter, and had an energy equivalent of 2600 calories, while his corn diet contained 96 grams protein, 617 grams carbohydrate, 64 grams fat, 26.45 grams mineral matter, and furnished 3450 calories. Camurri calls attention to the small relative amounts of sodium and calcium furnished by certain dietaries. The figures which we have calculated for the salt intake would appear to indicate that in this particular our diet was adequate and well balanced.

Composition of the Urine. The discussion of the urine can best be prefaced by the general statement that the chemical composition of the urine in pellagra does not markedly differ from what one might observe in other individuals of a similar physical condition, except in one particular, the increase in the quantity of the bodies derived from intestinal putrefaction—namely, the ethereal sulphates, and especially the indican. It is perhaps of some significance that a few hyalin casts were observed in 6 out of the 14 cases, while in 2, traces of albumin were detected.

The volume of urine eliminated and the specific gravity gave figures such as one might have anticipated with the fluid and food intake, the average volumes varying between 300 and 1800 c.c., with specific gravities of 1.029 to 1.013. As shown in Table II, the figures for total acidity, chlorides, phosphates, inorganic sulphates, neutral sulphur, for the mineral elements, calcium magnesium, sodium, and potassium (figures for sodium and potassium not included in table) are such as one might expect under the given dietary conditions, and the same may be said in regard to the various nitrogenous constituents.

[24] Report of the Pellagra Commission of the State of Illinois, 1911, p. 197.

TABLE II.—Summary Table. Average Daily Composition of the Urine.[25]

Patient.	Severity of condition.	Sex.	Age.	Wt. at begin'g of exper't.	Weight at end of exper'nt.	Average weight	Length of experiment.	Date, 1912.	Volume of urine.	Specific gravity.	Qualitative and Microscopic examination of urine.	Total N.	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Undetermined N.	Creatinin coefficient.
			Yrs.	Lbs.	Lbs.	Kgms.			C.c.			Gms.	Gms.	Gm.	Gm.	Gm.	Gm.	Gms.	
1—J. A.	Moderately severe: chronic	M.	60	143	145	65.3	9	June 14 to 23	912	1.019	Occasional granular casts, occasional leukocytes.	9.40	7.68	.51	.08	.36	.02	0.75	5.5
2—M. F.	Moderately severe; chronic	F.	17	76	75	34.2	9	June 9 to 18	676	1.023	Faint trace of albumin on several occasions, moderate number of pus cells.	7.74	6.75	.25	.06	.20	0	0.48	5.8
2—M. F. Period 2	Moderately severe; chronic	F.	17	78	82	36.3	7	June 29 to July 6	877	1.020	Negative.	7.25	6.07	.30	.05	.22	0	0.61	6.1
3—M. McH.	Severe; acute	F.	37	88	85	39.0	10	June 9 to 19	304	1.028	Moderate number pus cells.	5.89	4.73	.33	.06	.21	.04	0.52	5.4
3—M. McH. Period 2	Severe; acute	F.	37	85	86	38.1	7	June 29 to July 6	318	1.029	Moderate number pus cells.	4.87	3.85	.21	.07	.22	.01	0.51	5.8
4—C. T.	Mild; chronic	F.	40	121	122	54.9	9	July 7 to 16	1439	1.018	Negative.	9.47	7.75	.50	.08	.35	.02	0.77	6.4
5—R. N.	Moderately severe; chronic	F.	32	87	88	39.7	9	July 7 to 16	1198	1.019	Occasional hyaline cast on one day.	8.05	6.09	.41	.08	.23	.09	1.15	5.8
6—M. L.	Moderately severe; chronic	F.	36	94	100	43.8	9	July 21 to 30	1256	1.019	Negative.	10.71	8.94	.56	.09	.30	0	0.82	6.9
7—E. C.	Moderately severe; acute	F.	20	145	150	66.9	7	August 5 to 12	1496	1.014	Occasional hyaline casts on two days.	8.08	6.50	.41	.13	.33	.01	0.70	4.9
8—M. T.	Mild; acute	F.	18	116	118	53.1	7	August 5 to 12	1444	1.017	Occasional hyaline casts on one day.	10.62	9.08	.49	.13	.36	0	0.56	6.8
9—L. G.	Moderately severe; chronic	F.	28	114	118	52.0	8	August 17 to 25	1393	1.015	Trace of albumin on first three days and occasional hyaline casts on first five days.	9.12	7.55	.48	.11	.26	.03	0.69	5.0
10—M. S.	Severe; chronic	F.	28	89	91	41.3	10	August 17 to 27	839	1.023	Negative.	8.64	7.24	.47	.11	.23	0	0.59	5.6
11—B. B.	Mild; chronic	F.	33	90	94	41.7	7	August 23 to 30	987	1.017	Moderate number pus and red blood cells observed on several days and an occasional hyaline cast on one day.	8.80	7.59	.41	.05	.21	.02	0.52	5.0
12—A. N.	Mild; acute	F.	43	91	95	42.2	7	September 12 to 19	1833	1.013	Negative.	12.88	10.92	.35	.05	.25	0	1.31	5.9
13—C. McC.	Severe; chronic	F.	35	70	72	32.0	2	September 18 to 20	646	1.019	Many pus cells.	9.45	7.66	.67	...	.14	.11	...	4.4

[25] The tables of the individual metabolism studies from which these average figures have been computed will be included in the preliminary report of the Pellagra Commission and the authors' reprints of this paper. For the sake of brevity they have been omitted here.

TABLE II (CONCLUDED).—Average Daily Composition of the Urine.

Patient.	In percentage of total nitrogen.						Urea.	Ammonia.	Uric acid.	Creatinin.	Creatin.	Total acidity terms n/10 acid.	Calcium as CaO.	Magnesium as MgO.	Chlorides as NaCl.	Phosphates as P_2O_5.	Inorganic sulphates as SO_3.	Ratio ethereal: Inorganic SO_3.	Ethereal sulphates as SO_3.	Neutral sulphur as SO_3.	Indican (indoxyl-potassium-sulphate).
	Urea N.	Ammonia N.	Uric acid N.	Creatinin N.	Creatin N.	Undetermined N.															
							Gms.	Gm.	Gm.	Gm.	Gm.	C.c.	Gm.	Gm.	Gms.	Gms.	Gms.		Gm.	Gm.	Mgms.
1	81.7	5.4	0.9	3.8	0.2	8.0	16.5	.61	.24	.97	.06	429	.18	.13	6.08	2.01	1.352	1 to 6	.207	.213	151
2	87.2	3.2	.8	2.6	...	6.2	14.5	.30	.18	.54	0	303	.16	.08	5.14	1.85	1.067	1 to 8	.126	.203	97
2	83.7	4.1	.7	3.0	...	8.5	13.0	.36	.15	.59	0	332	.20	.07	7.88	2.04	1.064	1 to 11	.098	.263	48
3	80.3	5.6	1.0	3.6	.7	8.8	10.1	.40	.18	.57	.12	262	.14	.08	1.73	1.35	.705	1 to 7	.097	.122	69
3	79.1	4.3	1.4	4.5	.2	10.5	8.3	.26	.21	.59	.03	195	.09	.05	3.21	1.32	.577	1 to 5	.122	.154	91
4	81.8	5.3	.8	3.7	.2	8.2	16.6	.61	.24	.94	.06	300	.27	.18	14.05	2.09	1.332	1 to 7	.194	.193	208
5	75.7	5.1	1.0	2.9	1.1	14.2	13.1	.50	.24	.62	.28	315	.15	.12	14.07	2.16	1.150	1 to 20	.059	.168	43
6	83.5	5.2	.8	2.8	...	7.7	19.2	.68	.27	.81	0	257	.16	.07	12.90	1.88	1.635	1 to 11	.149	.203	45
7	80.4	5.1	1.6	4.1	.1	8.7	13.9	.50	.39	.87	.03	353	.39	.25	8.98	2.17	1.189	1 to 8	.147	.250	21
8	85.5	4.6	1.2	3.4	...	5.3	19.5	.60	.39	.97	0	339	.26	.23	9.83	2.56	1.727	1 to 11	.161	.280	88
9	82.8	5.3	1.2	2.9	.3	7.5	16.2	.58	.33	.70	.09	348	.15	.18	9.40	1.92	1.275	1 to 6	.203	.233	95
10	83.8	5.4	1.3	2.7	...	6.8	15.5	.57	.33	.62	0	264	.33	.09	9.46	2.12	1.274	1 to 11	.117	.279	23
11	86.2	4.7	.6	2.4	.2	6.9	16.3	.50	.15	.57	.06	413	.22	.12	6.94	2.21	1.370	1 to 11	.126	.270	71
12	84.8	2.7	.4	2.0	...	10.1	22.7	.43	.15	.67	0	461	.30	.30	8.71	3.36	2.156	1 to 17	.124	.446	65
13	81.0	7.1	...	1.5	1.2	....	16.4	.81	...	.37	.35	367	.25	.09	4.50	2.17	1.462	1 to 8	.181	.208	240

TABLE III.—Average Daily Food Intake, with Nitrogen Balance.

Patient.	Protein.	Fat.	Carbohydrates.	Calories.	Calcium as CaO.	Magnesium as MgO.	Sodium as Na_2O.	Potassium as K_2O.	Phosphates as P_2O_5.	Chlorides as Cl.	Food N.	Urinary plus fecal N.	N balance.	Approximate daily change in weight.
	Grams.	Grams.	Grams.		Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Grams.	Kilogram.
1—J. A.	79	126	260	2490	2.0	0.4	3.3	3.0	3.4	4.3	12.6	10.4	+2.2	+.10
2—M. F.	56	89	174	1720	1.8	0.3	2.7	2.6	2.7	3.6	8.9	8.3	+0.6	—.05
2—M. F.	78	103	315	2590	2.1	0.5	4.0	3.5	3.9	5.2	12.5	8.4	+4.1	+.26
Period 2														
3—M. McH.	31	36	122	940	1.2	0.1	0.8	0.1	1.7	1.4	5.0	6.4	—1.4	—.14
3—M. McH.	45	70	182	1540	1.3	0.2	2.1	2.1	2.0	2.9	7.2	6.2	+1.0	+.06
Period 2														
4—C. T.	79	98	278	2310	2.4	0.4	6.5	3.4	3.7	8.2	12.7	11.0	+1.7	+.05
5—R. N.	81	125	285	2590	2.4	0.4	7.1	3.3	3.9	8.9	12.9	10.4	+2.5	+.05
6—M. L.	91	134	281	2700	2.5	0.4	7.3	3.8	4.0	9.0	14.5	11.5	+3.0	+.30
7—E. C.	83	153	328	3020	2.3	0.5	4.6	4.0	3.8	6.8	13.3	9.9	+3.4	+.32
8—M. T.	88	77	372	2530	2.0	0.5	3.7	4.0	3.7	5.0	14.0	12.1	+1.9	+.13
9—L. G.	87	117	288	2550	2.3	0.4	4.4	4.0	3.8	6.5	13.9	10.6	+3.3	+.23
10—M. S.	76	109	261	2330	1.9	0.4	4.9	3.6	3.4	6.3	12.1	9.7	+2.4	+.09
11—B. B.	101	124	280	2640	2.6	0.5	4.2	4.3	4.4	5.3	16.1	11.1	+5.0	+.26
12—A. N.	113	131	339	3000	2.9	0.5	5.0	4.6	5.0	6.3	18.0	14.3	+3.7	+.26
13—C. McC.	106	125	190	2310	3.2	0.4	4.1	3.9	5.1	5.1	16.9	12.2	+4.7	+.45

TABLE IV.—Average Daily Composition of the Feces.

Patient.	Moist feces.	Air dry feces.	Moisture.	Nitrogen.	Nitrogen.	Protein utilization.	Ether extract.	Ether extract.	Fat utilization.	Carbohydrate as glucose.	Carbohydrate as glucose.	Carbohydrate utilization.	Ash.	Ash.	Calcium as CaO.	Magnesium as MgO.	Phosphates as P_2O_5.	Chlorides as Cl.	Indol.	Skatol.
	Gms.	Gms.	Per cent.	Per cent.	Gms.	Per cent.	Gms.	Per cent.	Per cent.	Gms.	Per cent.	Per cent.	Gms.	Per cent.	Gms.	Gm.	Gms.	Gms.	Mgms.	Mgms.
1—J. A.	103	21.6	79	4.67	1.01	92	6.9	31.9	94	.6	2.57	99.8	4.49	20.8	1.40	.25	1.08	.23	0	28
2—M. F.	56	13.7	76	3.71	.51	94	3.2	23.2	96	.4	2.77	99.8	3.06	22.3	1.26	.18	.71	.06	0	2
2—M. F.	90	23.6	74	4.81	1.13	91	2.7	11.4	98	.9	3.62	99.7	4.95	21.0	2.00	.31	1.01	.11	3	3
Period 2																				
3—M. McH.	59	9.7	84	5.53	.54	90	2.1	21.7	94	.2	2.57	99.8	2.16	22.3	.80	.12	.62	.15	2	9
3—M. McH.	182	22.0	88	6.27	1.36	81	3.2	14.6	95	1.7	7.57	99.0	3.96	18.0	1.08	.26	.76	.42	7	7
Period 2																				
4—C. T.	113	24.4	78	6.10	1.49	88	4.5	18.3	95	.6	2.53	99.8	5.05	20.7	1.94	.33	1.39	.38	5	10
5—R. N.	233	36.4	84	6.45	2.35	81	2.9	8.0	98	3.3	9.00	99.0	5.68	15.6	2.17	.35	1.17	.85	14	0
6—M. L.	73	19.0	74	3.97	.75	94	4.5	23.7	97	.8	4.14	99.7	4.52	23.8	1.75	.34	1.44	.14	0	1
7—E. C.	148	28.6	79	6.43	1.84	87	6.4	22.2	96	1.1	4.05	99.6	4.49	15.7	1.70	.20	1.16	.43	0	16
8—M. T.	129	23.1	82	6.46	1.49	89	4.4	19.2	94	.9	4.00	99.8	3.74	16.2	1.49	.25	.97	.33	3	12
9—L. G.	200	31.0	85	4.75	1.47	89	10.9	35.2	91	1.2	3.90	99.6	5.86	18.9	1.99	.33	1.49	.26	11	34
10—M. S.	195	22.8	88	5.96	1.10	91	3.3	14.3	97	1.3	5.67	99.5	4.33	19.0	1.44	.30	.88	.40	2	19
11—B. B.	367	41.1	89	5.55	2.28	86	10.5	25.5	92	1.4	3.36	99.5	7.15	17.4	2.40	.40	1.60	.67	21	51
12—A. N.	147	27.4	81	5.13	1.41	92	5.3	19.4	96	1.2	4.53	99.6	5.84	21.3	2.65	.43	1.03	.41	Faint	Reaction
13—C. McC.	772	42.0	95	6.44	2.70	79	11.1	26.3	89	Trace	Trace	100.0	11.47	27.3	2.47	.36	2.44	2.19	0	0

The elimination of total nitrogen, urea, ammonia, uric acid, and creatinin is perhaps slightly below the so-called normal, though the constituents dependent upon exogenous factors, namely, the urea and ammonia, are in accord with the diet, and those of endogenous origin, namely, the uric acid and creatinin, are such as might be observed in other individuals of similar physical condition. Since Folin[26] first considered the distribution of the nitrogenous constituents in normal urine a large amount of work has been done on this subject. The large amount of data collected in the publications of the Referee Board[27] is unusually good confirmation of the statements of Folin in this particular. Although our data for the percentage of ammonia and undetermined nitrogen are slightly above the so-called normal figures and the other constituents slightly below, these differences are readily interpreted as due to the diet and the physical condition of the patients. As Folin has so well shown, with a reduction of the nitrogen-intake the urinary constituents of exogenous origin necessarily form a smaller percentage of the total nitrogen, and our figures for urea nitrogen, generally 83 per cent., are in accord with the nitrogen of the food. As the endogenous metabolism of the body was at a low state of activity, due to the rather poor physical condition of the individuals, we would hardly expect the uric acid (purin-free diet) and creatinin nitrogen to form an increased percentage of the total nitrogen. On the contrary the percentage of nitrogen in this form is rather below the normal.

An examination of the absolute amounts of the various nitrogenous constituents eliminated by the different individuals shows that in general the urea varied between 10 and 20 grams, the ammonia between 0.3 and 0.8 gram, the uric acid between 0.15 and 0.39 gram, and the creatinin between 0.4 and 1 gram. The absolute amount of the undetermined nitrogen in general falls within normal limits, though, as mentioned above, it forms a rather high percentage of the total nitrogen. In Cases 2 and 12, however, the figures are considerably higher than those found in other cases of the series.

The creatinin elimination is below normal in all cases, this fact being particularly well shown by the creatinin coefficients. Normally, coefficients of 7 to 11 are found, while here the figures vary between 5 and 7. As recently discussed by one of us[28] (Myers), the creatinin elimination is lowered in conditions associated with decreased body efficiency. This general inefficiency is further brought out by the fact that 10 out of the 14 cases eliminated creatin, though in only 2 cases was it present in large amount.

The elimination of the mineral constituents hardly requires

[26] Amer. Jour. Phys., 1905, xiii, 66.
[27] United States Dept. of Agric., Report No. 88, 1909, and No. 94, 1911.
[28] Amer. Jour. Med. Sci., 1910, cxxxix, 256.

further comment, except for that part containing an organic radicle, namely, the ethereal sulphates. Certain of the facts in this connection are best brought out in Table I, in which the data are arranged in order of the amounts of indican eliminated. The absolute amounts of the ethereal sulphates appear to be increased in a few instances, in which case there exists a low ratio to the ethereal sulphates. This is especially pronounced in the cases of anacidity, in which very large amounts of indican were eliminated. Here the indican appears to parallel the total ethereal sulphates, but apparently for the reason that the indican forms a considerable part of the total ethereal sulphates. The low ratio of inorganic to ethereal sulphates was observed in the cases reported by Camurri.

Composition of the Feces. The examination of the feces as shown in Table IV revealed widely varying conditions as to volume and consistency—watery stools, soft stools, well-formed stools, and hard stools—the average daily elimination amounting to from 60 to 700 grams of moist feces and 20 to 40 grams of air-dried feces, the moisture varying between 75 and 95 per cent. The microscopic examination of the feces has not yielded data of special significance, though in certain cases evidence of digestive inefficiency has been observed, and in some cases considerable mucus, probably in part due to the diarrhea. In several instances strongly positive fermentation tests with Schmidt tubes have been observed, notably in Case 3 (M. McH)., period 2, though the estimation of the carbohydrate content of the feces ought to be a more adequate criterion. The daily fecal nitrogen was found as low as 0.5 gram where the nitrogen intake was low, and as high as 2.7 grams in the reverse condition, accompanied by severe diarrhea. These figures fall within the normal limits, however, and the percentage of nitrogen in the air-dried feces cannot be said to be excessive, though perhaps slightly above the normal average in a few cases. In 3 cases (Case 3, period 2, Case 5, and Case 13) the so-called protein utilization was below the other figures observed, but probably in part due to the diarrhea. The daily fat eliminated varied from 2 to 11 grams, with percentages of the air-dried feces ranging between 8 and 35 per cent. The fat utilization was good in all cases, though the figures for Cases 9, 11, and 13 were slightly below that observed in other cases. The figures for the carbohydrate were from direct estimation, and are therefore much more reliable than the results generally reported as determined by difference. The tabulated data show that the utilization was 99.5 to 99.8 per cent. in all but 2 cases (Case 3, period 2, and Case 5), where the utilization was 99 per cent. and the percentage content in the feces 7.6 and 9 per cent. These results show quite conclusively that the ability of the pellagrins to absorb their food is only slightly if at all impaired and that this is in part due to the diarrhea. The data on the feces

reported by Camurri bring out similar points, though he has only five sets of average figures with which to make comparison.

The examination of the feces has included quantitative determinations of calcium, magnesium, phosphates, chlorides, as shown in Table IV, and also of sodium and potassium. These data have not revealed any apparent derangement of mineral metabolism, though certain interesting relationships have been brought to light, which will be presented in a subsequent paper.

The feces of pellagrous individuals have a most characteristic aromatic odor, and the estimations of the indol and skatol would indicate that this odor was due to the large amounts of these aromatic bodies found to be present. Normally only traces of these bodies are present, and from the investigation of Herter[29] and also of one of us[30] (Myers), with Fisher and Diefendorf, the amounts detected, especially of skatol, may be regarded as decidedly abnormal and indicative of peculiar bacterial conditions in the intestine. When these results are compared with the acidity determination in the gastric juice, some relation between the amount of skatol formation and anacidity is apparent.

SUMMARY. The ability of individuals suffering from pellagra to utilize the various foodstuffs as indicated by our series of fifteen experiments appears to be only slightly if at all below the normal.

The elimination of mineral and nitrogenous constituents in the urine is such as would be anticipated under the dietary and physical conditions of the individuals. A lowered physiologic efficiency is indicated by the low creatinin coefficients and the elimination of small amounts of creatin in the urine. The presence of a few hyalin casts in about 45 per cent. of the cases points to some possible irritation of the kidney.

Anacidity is a condition common in pellagra, found in eight of our fourteen cases. It is generally associated with an entire absence of pepsin, or with pepsin in only very minute quantities.

Individuals suffering from pellagra show a marked indicanuria, which is excessive in the cases with gastric inefficiency. Though the ethereal sulphate hardly parallels the indoxyl-potassium sulphate, the quantities eliminated are much higher where anacidity exists and they furthermore hold a higher ratio to the inorganic sulphates.

The feces contain decidedly abnormal amounts of indol and skatol, especially the latter.

The presence of excessive amounts of indican in the urine, associated with a high elimination of ethereal sulphates, when considered in connection with the abnormal amounts of indol and skatol in the feces, points to some unusual bacterial conditions in the intestine. From the data at hand this putrefaction would appear to take place rather high up in the intestine.

[29] Bacterial Infections of the Digestive Tract, 1907, p. 239.

[30] Zentralbl. f. Stoffwechsels, 1908, ix, 849; Amer. Jour. Insanity, 1909, lxv, 607.

ACUTE SUPPURATIVE LYMPHADENITIS, ABDOMINAL, DUE TO A DIPLOSTREPTOCOCCUS: AUTOPSY.

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Within the last two years the number of infections due to diplococci and diplostreptococci has greatly increased. Many of these infections are quite serious and not a few are fatal. The organisms described in various parts of the country are similar and likewise are the diseased conditions produced. That these infections are on the increase cannot be explained on the basis that they were not recognized heretofore because of the unusual sites of the lesions.

In this city and surrounding country, during the spring of 1912, there occurred many infections of this nature. The majority of the lesions were located in the cervical lymph nodes and the periglandular tissue. Practically all of them followed throat infections. Many cases subsided without suppuration, but in a number drainage was necessary. The pus from all of these cases showed enormous numbers of short chain diplostreptococci which were Gram positive. They grew on blood serum as small isolated white colonies. On blood agar quite a large hemolytic ring was produced around each colony. The organisms lived only a few days on artificial media, and the colonies rarely developed larger than the head of a pin.

On May 12, 1912, I was called to see the patient, Mr. R. S. The history as taken by Dr. F. G. Nifong, in whose surgical service the case occurred, is as follows:

The patient was aged forty-one years; American; farmer; male; white; widower.

Family History. Father living and in good health, eight-one years old. Had seven brothers and two sisters. One sister and two brothers are dead. One uncle died from cancer.

Previous History. Never had any serious sickness in his life. Three years ago he fell from a tree and sustained some internal injury.

Present Trouble. On May 1 he suffered epigastric pain and a little nausea after breakfact. He ate his dinner and suffered severely after it. The next day he called Dr. R. W. Berry, of Mexico, Missouri. Castor oil was administered and the bowels moved freely. Pain continued, and on May 12 the patient visited Dr. Berry in Mexico, which is fifteen miles from his home. At this time the patient was suffering from severe pain in the region of the gall-bladder, and there was some jaundice. After staying one night in Mexico he returned to his farm. He suffered greatly

in returning, and from this time on he had increasing pain. Since that time he has suffered a great deal, especially after eating, and has been rapidly declining.

Physical Examination. The chest is negative. There is marked muscle resistance all over the abdomen, and especially over the epigastric region. A small area just below the umbilicus was more tender than other parts of the abdomen.

The temperature upon admission to the hospital was 101°, but dropped to normal a few hours after being put to bed. From that time until death his temperature never registered over 100. The white blood count was 14,000. The pulse ranged from 68 to 78. Throughout the illness the patient perspired very freely.

On May 27 the patient was operated and the following notes were given by Dr. Nifong: Median incision. Could find nothing in the colon or stomach. The appendix was removed and showed some evidence of inflammation. After raising the stomach and colon much induration of the mesentery and great enlargement of retroperitoneal and mesenteric lymph nodes were noted. This condition was especially noticeable in the mesojejunum. The abdomen was then closed.

The patient gradually grew weaker, and died June 6. An autopsy was immediately performed and the following is a summary of the findings: The body of a greatly emaciated white man. The skeletal system is moderately heavy and the musculature very light. The subcutaneous fat is practically absent. The lungs are free from adhesions, containing air throughout. They are normal except for a little scarring at the right apex. The heart is normal, all of the valves are delicate. The spleen is normal. All of the mesenteric and retroperitoneal lymph nodes are greatly enlarged and are quite soft. Upon section a greenish-yellow pus escapes. The largest of these lymph nodes are in the duodenal and ileocecal regions. The mesentery is indurated. The liver is somewhat enlarged, and upon section shows numerous abscesses varying in size from a pinpoint to 1.5 cm. in diameter. The abscesses are filled with a greenish-yellow pus and are located in connection or in apposition to the bile ducts. The gall-bladder is normal. The kidneys are slightly enlarged, and on section are found to contain a great deal of blood.

Anatomic Diagnosis. Acute suppurative lymphadenitis affecting practically all of the abdominal and pelvic lymph nodes. Acute suppurative hepatitis, with abscess formation.

A histologic study of the tissues showed the condition to be of an acute suppurative type. Examination of the smallest hepatic abscesses showed that they were not in connection with the bile ducts but in the tissue immediately surrounding the ducts. The infection had apparently been conveyed by the lymphatics. Smears from the pus showed enormous numbers of organisms belonging to

the diplococcus or diplostreptococcus type. These organisms occurred in pairs and in chains of four or six. They were Gram positive.

After the autopsy an attempt was made to find if the individual had suffered from a throat infection previous to this illness. He mentioned no such trouble in the histories given to Dr. Berry or Dr. Nifong. Whether or not the condition was secondary to a throat infection I am unable to say. The organism causing it was the same as occurred in the cervical lymphadenitis cases and the lesions were of the same kind. Surely a primary lesion had occurred somewhere in the respiratory or alimentary tracts, but it could easily have disappeared before the examinations were begun, or was so slight as to escape the notice of the patient.

OCCUPATIONAL BRASS POISONING: BRASS-FOUNDER'S AGUE.

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Introduction and Definitions. 1. *The Alloys.* Brass is an alloy composed of copper and zinc. Fine brass or red brass contains two parts of copper and one part of zinc. However, as these two metals combine in practically all proportions many alloys are possible. As zinc is by far the cheaper of the two component metals its percentage in the alloy is likely to be much increased until a so-called yellow brass is produced in which the zinc component may be from 40 to 50 per cent. This the workmen style "cheap yellow brass."

Bronze is an alloy consisting of copper and tin. Usually the copper component is about nine parts to one part tin. In the industry, however, red brass is very often styled bronze, although zinc is the other component instead of tin. It is only rarely that these two or three metals are used exclusively in the particular alloy to be made, but for the purpose of conveying certain physical properties to the casting, certain other metals are added, such as lead, aluminum, phosphorus, nickel, and antimony. There are some threescore of these various compositions which are well known and are made up for certain purposes, brass, bronze, German silver, aluminum alloys, type-metal, etc.

In the usual foundry practice these various alloys are not made by putting in certain proportions of the various metals, but, as a rule, a large percentage, from one-third to one-half on the average, of scrap brass, copper, and bronze, consisting of all sorts and com-

positions of metal, gathered up usually by junk dealers, is melted down, and then a small portion of the proper copper, zinc, or nickel ingot added to arrive at an approximate composition. In fact, a large amount of the so-called virgin copper, zinc, etc., used is bought from refiners of scrap metal, and the composition is very uncertain. Certain foundries make a specialty of yellow brass castings, others of red brass or bronze castings, others of German silver, etc., while the refiners are concerned with the handling of all of these metals, and usually with a large amount of lead.

Consequently, the brass-manufacturing industry, or more properly the non-ferruginous metal-working trade, is engaged in the handling of large amounts of copper, zinc, and tin, while it must not be overlooked that lead, antimony, nickel, phosphorus, arsenic, and cyanide compounds sometimes enter into these industries, as well as the handling of concentrated and fuming acids, muriatic, sulphuric, nitric, and hydrofluoric.

Finally, scrap metal, old boiler tubes, etc., by the action of air and moisture, may be covered with more or less poisonous oxides and carbonates by which ignorant workmen may be poisoned, both by handling and breathing the metallic dusts. In addition to the metals above named as entering into the composition of various brass alloys, the salts with which they are combined to a limited extent require some notice, such as the oxides, the sulphides, the sulphates, silicates, and nitrates.

2. *Pseudo-brass Poisoning.* Direct toxic effects due to any of these alloys of zinc, copper, etc., in the cold metallic state, when these come in contact with the tissues of the body, are of mechanical traumatic significance only, with whatever possibilities subsequent infection may add. As is well known, also, the salts of some of these metals have a local effect, which is astringent to caustic. The inhalation of dust of any of these alloys, as, for instance, among polishers, buffers, and grinders, in the industry does not produce the symptom-complex known as "brass-founder's ague," which will be described shortly. An investigation made by the Illinois Commission on Occupational Diseases,[1] 1910, among some 2000 brass-polishers and buffers, failed to discover any affections peculiar to brass dust itself, nor did it appear to be any more harmful than iron dust to iron workers, or stone dust to masons and stone-cutters. It is true that these workers suffer from chronic bronchitis in proportion to their exposure, and rapidly develop respiratory affections. According to Lehmann and Saito[2] the

[1] Report of Commission on Occupational Diseases to His Excellency Governor Charles S. Deneen, Illinois, January 1, 1911. Copies obtainable from State Factory Inspector, Chicago.

[2] Experimental Untersuchungen über die quantitative Absorption von Staub durch Tiere bei genau bekannten Staubgehalt der Luft, Arch. f. Hyg., 1912, lxxv, S. 134; Lehmann, Saito and Gfroerer, Ueber die quantitative Absorption von Staub aus der Luft durch den Menchen, ibid., S. 152; Murgia, E., Ricerca sull 'assorbimento e sulla tossicita di alcuni minerali di zinco, La Clinica Moderna, 1906, xii, 316–19.

great bulk of inspired dust finds its way into the stomach, not into the lungs as has been confidently assumed. Obviously, inhaled dusts are collected in the upper respiratory passages, and either discharged directly therefrom or swallowed, while less than a quarter reaches the lungs. This would be particularly true of these heavier metallic dusts.

The dusts from alloys rich in copper generally produce in workers green-stained hair, a greenish deposit on the teeth and gums, and a green tint to the perspiration, which may persist briefly even after a thorough bath, but all of these are without direct effects upon the health. Such findings are much more pronounced among copper workers than brass-workers. Literature teems with references to the relative harmlessness of copper upon the human organism. It has been found accumulated in all the organs of the body, and even in the bones of former copper-workers, which have shown a green discoloration when later removed from graves. About seventy-five coppersmiths interviewed in Chicago were found to be uniformly healthy. Many of these were old men who had been at the trade from thirty to fifty years. This agrees with the observations of others.

"Brass itch" is a rather common condition among brass-polishers which is due to the slight irritation of brass dust, combined with habits of uncleanliness, and is more prevalent in hot weather. Brass-foundrymen, however, are singularly free from these green discolorations of hair, teeth, perspiration, etc., for the obvious reason that they are very little exposed to brass dusts.

3. *Limitation of Brass Poisoning.* Brass poisoning may then be narrowed down, even in the industries, to those exposed to the inhalation of fumes arising from molten brass within the brass foundry. Hence, the affliction "brass poisoning" is unknown outside of the industry. Brass in any condition of temperature short of that of the recent vaporous state of its components, produces no intoxication peculiar to itself.

4. *Brass-founder's Ague* (brass chills; Giessfieber; Staubfieber; fievre des fondeurs; Gelbgiesser. The workmen use cruder terms, such as "the shakes," "smelters' shakes," and "zinc chills"). This is the theme of interest in occupational brass poisoning. Without question it is a symptom-complex peculiar to the human being. Investigators to date have failed to produce the ague features in lower animals either by inhalation of brass fumes, intratracheal insufflations, ingestion or instillations or injections.

"Brass-founder's ague" may be defined as an acute malaria-like syndrome of chill, fever (sometimes), and sweat, appearing a few hours after the inhalation, for a few minutes or longer, of the vapors or fumes arising from molten brass, or from the fumes of pure zinc alone,[3] affecting only or mostly those unaccustomed

[3] K. B. Lehmann, Giess-oder Zinefieber, Arch. f. Hyg., 1910, ed. lxxii, S. 358–381.

to such exposure; further characterized by the development of a form of temporary immunity, and absence of immediate serious or fatal consequences, a lack of definite pathology, and the probability of the development of non-resistance to secondary affections, which account for the increase in the morbidity and mortality of persons so exposed.

The symptoms, which appear usually several hours after the pouring of brass or after an exposure to the metallic smoke arising from the metal, set in with a dry, parched throat, an irritating and unproductive cough, a metallic taste, a feeling of constriction in the chest, lassitude, more or less anorexia, followed occasionally by nausea and sometimes emesis. Within one to four hours chilly sensations begin to be noticeable while a slight dull headache develops. The workman usually lies down or takes to his bed. The chills rapidly increase into a distinct rigor, which may last from a half to two or three hours. No amount of external heat or blankets appears to lessen the rigor. Also, there is a great desire to imbibe hot drinks and stimulants. Accompanying the chills and rigor there are usually muscular cramps and sharp joint pains. The victim feels that he is deathly sick. These symptoms end almost by crisis, and are followed at once by a most profuse perspiration, while the prostration lasts for several hours longer. In many cases there is a distinct rise in temperature during and following the chills, but it is not constant and may be subnormal. It does not usually mount high. Following the stage of perspiration, the victim, quite prostrated, falls into a deep and restful sleep, from which he awakens with no remaining symptoms of his recent experience other than a little exhaustion, perhaps a metallic taste in his mouth, and a temporary loathing of food. The entire attack usually lasts from five to twenty hours; seldom longer.

The pulse during the chill is small and rapid (120 to 130 per minute). The respiratory rate is not much affected. The blood findings during and after a chill have been reported by most investigators as entirely normal, although some have found a slight leukocytosis. The urine after a severe chill invariably shows albumin and casts, which clear up within a day or so. In 1906, J. Sigel[4] proved the presence of zinc in the urine. This has since been verified by Lehmann, Arnstein, and others. Sigel also proved the absence of carbon monoxid hemoglobin as an etiological factor by spectroscopic examination of the blood. Weyl[5] comments on associated splenic enlargement. Arnstein[6] emphasizes the large amount of zinc found in the feces.

[4] Das Giessfieber und seine Bekämpfung mit besonderer Berüchsichtigung der Verhältnisse in Würtemberg, Vrtjschr. f. gerichtl. Med., 1906, xxxii, S. 174.

[5] Handbuch der Arbeiterkrankheiten, 1908, note, S. 114.

[6] Arnstein, A., Beiträg zur Kenntnis des Giessfieber, Wiener Arbeiten aus dem Gebiete des sozialen Med., 1910, I. Folge, S. 49–59.

There are many conditions which seem to influence the onset and severity of brass chills. The newer workmen, or those who have returned to work after a week's vacation, perhaps only after a day or so off, as over Sunday, are the most liable. Unless the exposure to the metallic smoke and vapors has been unduly severe, the workman continues at his vocation all day without noticing untoward health effects. It is usually after leaving the workshop at night that the sickness comes on. Many state that as soon as the cold outside air strikes them the chill is inaugurated. Hence the chills are far more common in the winter than in the summer. Many state that while riding in the street cars after the day's labor, or perhaps on removing the clothes to go to bed in the evening after a previous period of indisposition, the chill begins. The men claim that it is because they breathe more vapors in the winter than in the summer that chills are much more frequent in this season. This is because, in an endeavor to keep warm while at work and to keep the furnaces and moulds from "chilling," the windows, doors, and skylights are kept practically closed; hence the fumes fail to escape through their usual routes of ventilation as they do in the summer season.

Brassman's ague occurs almost exclusively among workers in brass foundries, but also in foundries in which zinc, alone or alloyed, is heated to boiling. In Illinois the only process in vogue of reducing crude ores to recover the zinc is one of volatilizing the zinc in huge smelters—the Belgian process. Here an investigation showed that the men working around the smelters occasionally suffered from zinc chills, or "the shakes," as they were wont to call them. They are not as much exposed to the metallic fumes, however, as men who work in brass foundries. Brass chills do not occur in iron foundries nor in bronze foundries. Neither do they occur among galvanizers, the reason being obvious that in this latter process the zinc is only melted and is not ordinarily heated above its point of volatilization. The method of alloying is of great influence, as the frequency of the chill, other conditions remaining the same, is almost in direct ratio to the percentage of zinc contained in the alloy.

About 70 to 80 per cent. only of workmen seem susceptible to the vapors from brass or zinc and experience the chills. Hence some natural immunity seems to exist. Also a tolerance occurs in about 70 to 75 per cent. of workmen who work steadily at the trade. A further 20 to 25 per cent. sicken more or less regularly, but usually not severely. Only in very rare cases do these attacks occur so continually that a change of occupation is necessary. All factors which tend to lower natural vitality are predisposing to brass chills, especially alcoholism, poor quality of food, as is consumed by a large proportion of the foreign workmen, irregular hours, and excesses of all kinds. In addition, weak, anemic individ-

uals, young persons, and women are more subject to brass chills than are robust individuals.

According to Simon[7] brass-founder's ague is only an acute expression of a chronic malady, and one which rarely or never comes within the range or experience of practising physicians. This question of chronicity is still a disputed point.

5. *Health of Brass-founders.* "The moulders consider the fever so commonplace and matter-of-course—only a few having been exempt and many having had it as much as one hundred times and more—that they do not go or send to the physician on account of same. At all events, physicians, on this account, have rarely had the opportunity of observing brass-founder's ague," Weyl.[8]

According to Simon[9] the situation is the same in England, and we have found it to be similar in Chicago.[10]

In addition to brass-founder's ague, respiratory diseases are very common (chronic bronchitis and pulmonary tuberculosis), while older workmen invariably complain of gastro-intestinal symptoms, such as chronic dyspepsia, biliary trouble, occasionally gallstones; often they are slightly icteroid. Constipation is the rule among them and hemorrhoids are a common complaint. Pyorrhea alveolaris and carious teeth are common. The frequency of anemia, ill-nourishment, and emaciation has long been cited as characteristic of older brass-moulders.

The inducement to alcoholism among the workmen is great because of the chronic pharyngeal and laryngeal irritation from which they suffer. Most of the workmen resort to whisky, although only a few declare that it is antidotal. It is, unfortunately, a traditional remedy. There is no proof of its beneficial effects.

According to Tatham:[11] "They sustain a mortality from 'phthisis' which is in excess of that of 'occupied males' by 50 per cent., while they die more rapidly than the average from diseases of the nervous, urinary, and respiratory systems." Our investigations in Chicago in 1910, although not statistical upon this point, discovered a goodly number of young and middle-aged men invalidated by the ravages of consumption.

"If more proof were wanting of the unhealthiness of brass-casters, it would be afforded by the fact that a few years ago, though there were 1200 casters in Birminghan, there were not more than ten over sixty years of age, and in connection with the superannuation fund of the Amalgamated Brass Worker's Association, from which casters could at the age of fifty-five derive

[7] Oliver's Dangerous Trades, 1902, p. 460.
[8] Handbuch der Arbeiterkrankheiten, 1908.
[9] Loc. cit.
[10] Hayhurst, E. R., The Brass-moulder's Secret, The Survey, New York, 1911, No. 26, xxvi, 879–882.
[11] Oliver's Dangerous Trades, 1902, p. 135.

benefit, it is an appalling fact that there were only three men . . . enjoying this benefit" (Simon).

Practically only young men are found to be employed in the industry in Chicago. Employers gave as a reason for this that the older men (those over forty) became too slow or undependable for the work. The workmen themselves claimed that they were gradually incapacitated from the inhalation of brass fumes combined with the strain of piece-work. By no means the same condition was found to exist among iron-founders, who were engaged in the same identical processes. As is well known the latter continue at their trade until they reach a fair old age.

BIBLIOGRAPHY. Although the literature on the entire subject of brass-founder's ague is very scarce it is not my intention to enter upon more than a brief summary of it here. The affection was confused with malaria until the year 1830, when Thackrah,[12] in England, first described it as a separate affection peculiar to brass-workers. In 1845 it was recognized and described by Blaudet[13] in France. In 1858 Greenhow,[14] in England, on the basis of his researches, came to the conclusion that "Brass-pourers and doubtless all workmen who deal with zinc vapors are easily attacked with a disease similar to an intermittent fever of irregular type." In Germany, Schnitzer[15] was the first to call special attention to brass chills in 1862. In 1906 J. Sigel,[16] in Wurtemberg, Germany, sums up the entire literature concerning this peculiar malady and adds the results of his own investigation. In America a few articles have appeared in recent years, usually reports of individual cases, among them being one by Moyer and Lavin,[17] of Chicago, in 1904; also one by Pietrowiecz,[18] in 1904. The disease, as well as chronic symptoms of brass-workers, is also commented upon by George M. Kober,[19] of the President's Home Commission, 1908.

Recent literature deals particularly with the experimental side of this peculiar malady, and the investigations of Lehmann,[20] Arnstein,[21] and Kisskalt[22] have thrown considerable light upon its nature.

ETIOLOGY. The question of the exact cause of the ague-like symptoms seen among those exposed to brass fumes has been a matter of dispute since the time of Thackrah, some authors claiming it to be an expression of acute copper poisoning, others a zinc

[12] Essay on the Effects of Arts, Trades, and Professions on Health and Longevity, 1830.
[13] Annales d'hygiene et de méd. lég., 1845, xxxiii, 462.
[14] Med. Chir. Trans., 1862, p. 180.
[15] Preussiche Medic. Zeitung, 1862, S. 198.
[16] Loc. cit.
[17] Chronic Brass Poisoning, Brass-worker's Ague, Medicine, Detroit, 1904, p. 335.
[18] A Case of Brass-moulder's Ague, Jour. Amer. Med. Assoc., 1904, xliii, 465.
[19] Industrial and Personal Hygiene, 1908, p. 49.
[20] Loc. cit.
[21] Loc. cit.
[22] Ueber das Giessfieber und verwandte gewerbliche Metalldampfinhalationkrankheiten, Zeitschr. f. Hyg. u. Infectionkrank., 1912, lxxi, S. 472.

intoxication, others arsenical poisoning,[23] and still others have commented on the presence of lead, cadmium, etc., in the fumes. The question is a difficult one because of the number of contaminating metals and impurities encountered in the process of manufacturing brass.

The volatilization of the metals in making brass is accompanied by a display of blue-green flames, scintillating sparks, and marked deflagration, especially of the zinc component. A white smoke arises above the metals, out of which small snow-like flakes sublime. It is this whitish smoke and its sublimation products that are the cause of brass chills. Many analyses of this smoke and its products have been made, but no two authorities agree on the same findings, as might be expected from the inconstant composition of the alloys producing it. A typical analysis taken from *Dangerous Trades*, by Oliver, 1902, page 456, is as follows:

	Per cent.
Organic matter	39.42
Oxide of zinc	28.82
Oxide of iron	2.78
Copper	1.71
Silicates	9.14
Moisture	9.64
Other matter	8.49
	100.00

Analysis of a similar specimen made for the Illinois Commission on Occupational Diseases[24] gave:

	Per cent.
Zinc	44.9
Lead	0.8

Others have reported the presence of cadmium, nickel, sulphur, traces of arsenic, phosphorus, and other metals and acids.

Although zinc has always been held the metal chiefly to blame for brass chills, its necessary combination with copper has been stoutly maintained up to 1905, when Sigel[25] first showed brass chills occurring in foundries where no copper or iron could be demonstrated in the sublimation product. Sigel came to the conclusion that the chills were due to the entrance into the system of metallic zinc in the form of zinc dust and *in statu nascendi*.

In the fall of 1910 I found that so-called "zinc chills" existed among the zinc smelters of La Salle County,[26] Illinois. The raw ore used consists of zinc blende (sulphide of zinc). These ores contain no copper or arsenic, and only traces of iron, lead, manganese, and magnesium; 31 per cent. of sulphur is present, as well as oxides and silicates, leaving less than 1 per cent. of undetermined

[23] Von Jaksch, Vergiftungen, 1897, S. 184.
[24] Loc. cit.
[25] Loc. cit.
[26] Loc. cit.

matter. However, neither sulphur, silicates, nor any of the other metals present are known to produce a chill, fever, and sweat syndrome.

Lehmann[27] was the first to succeed in proving that the syndrome could be produced in man by burning chemically pure zinc. He further concludes that the affection is a direct or indirect zinc poisoning. "According to the very small traces of zinc which appear in the urine, to the symptom complex, and to the sudden cessation of the phenomena, the idea seems acceptable that a resorption of the cell contents (bacterial or epithelial), destroyed or changed by zinc, in the respiratory tract, may be the cause of the peculiar sickness. A complication of intoxication with an infection through the entrance of living bacteria is imaginable in the more severe cases, but certainly only as an exception. Zinc is inhaled only as zinc oxide not as zinc vapor."

Recently about the same symptom-complex has been observed in the case of the inhalation of the fumes of other metals, Armit[28] finding a similar syndrome in the case of the inhalation of nickel-carbonyl and cobalt fumes. Very little is known as to the actual inhalation of copper fumes, since, like nickel, its boiling point is very high. There is great likelihood, however, that the severe brass chills which workmen suffer in making German silver where it is necessary to fuse nickel (about 1500° C., which is above the boiling point of copper by 200° or 300°), are due as much to inhalation of copper fumes as to those of the associated zinc. Hansen,[29] a metallurgical engineer, cites some peculiar effects not unlike those due to zinc, which he attributes to copper fumes produced in an electrolytic process. When we consider the relatively low boiling point of zinc compared to that of all the other metals with which it is alloyed it is easy to see why these symptoms have been so closely associated with zinc, and not, at least in the industries observed in connection with other metals. Boiling points: Zinc 830° C.; copper, 1300° C.; lead, 1450° to 1600° C.; tin, 1600° C.; nickel, iron, and steel all over 1600° C. Melting points: Tin, 232° C.; lead, 327° C.; zinc, 419° C.; copper, 1080° C.; nickel and iron, about 1500° C. Brass itself melts at about 1000° C. Hence it is seen that, with the exception of mercury, whose boiling point is 357° C., but the dangers from the vapors of which are well known, zinc is the only supposedly innocent metal whose boiling point is commonly reached in the industries.

Kisskalt,[30] who has been impressed by the *rise in temperature*, occasionally observed in the brass-ague syndrome, has looked up the literature carefully in regard to other metals which have

[27] Loc. cit.
[28] Toxicology of Nickel Carbonyl, Jour. Hygiene, 1911, vii, 525–551, and viii, 565–600.
[29] Copper Poisoning, Metallurgical and Chemical Engineering, No. 2, ix, 67.
[30] Loc. cit.

been inhaled, ingested, and injected, and notes significant analogies. After a series of experiments upon rabbits he concludes as follows: "(1) Subcutaneous injections of zinc salts will produce fever; this may account for the same in brass-founder's ague. (2) Inhalation of mercury often causes fever in man and animals, as well as pronounced respiratory symptoms. (3) Also other heavy metals produce the phenomena of brass-founder's ague by inhalation. Vapors of heavy metals inhaled produce more similar symptoms than when taken up by other routes." At another point in his article he makes the following interesting observation: "For a long time it was considered that fever was produced by bacteria only; then it was found foreign proteins had the same effect; now heavy metals come to be added thereto. The effects of all seem to be the same. Heavy metals produce proteid precipitation and so 'denatured' protein occurs in the organism and this produces the fever. Zinc especially causes precipitation in unusual dilution."

In some recent experiments (not yet published) carried on under the Sprague Memorial Institute, Chicago, we have been able, by using Bertrand and Javillier's[31] calcium zincate method of isolating zinc, and Ganazzini's[32] basic urate of zinc test to verify its presence, to trace zinc, in the case of rabbits, which were exposed for as short a time as forty minutes to the inhalation of brass fumes, through the lungs (six hours afterward), and liver and kidneys (twenty-four hours afterward).

It is very probable that the peculiar toxicity of zinc is due, as Armit has found in the case of nickel carbonyl, to its being introduced in a gaseous form, perhaps zinc carbonyl, and that the zinc is deposited as a slightly soluble compound in a very fine state of subdivision over the immense area of the respiratory surface.

Scope of the Brass Industry. In brief this may be said to include all the non-ferruginous metal trades, since the brass furnace is used for melting and alloying practically all metals except iron and steel. Zinc is an almost universal constituent, both because it is cheap and because of the physical properties it bestows upon the alloy.

England, Germany, and France are all great centres of brass manufacture. In America, according to the Bureau of Census[33] the products of the industry exceed $100,000,000 in annual valuation, of which over 50 per cent. is controlled by Connecticut

[31] Sur une methode extrement sensible de precipitation du zinc, Bull. de la Soc. Chim. de Paris, 1907, 4a S. T. I., p. 63; Annales de Chimie An. Appl., 1907, T. II, p. 179, and Sur u methode pertant de doser de tres petites quantities du zinc, Compt. Rendu de l'Acad. des Scien., Paris, 1907, T. 145, 2 sém., p. 924.

[32] Ricerca qualitiva dello zinco e sua identificatione con una nuova reazione, 1909, Bollettino della Società Medico-Chirurgica di Pavia, xxiii, 72–90.

[33] Bureau of Census, United States, Department of Commerce and Labor, Special Reports, Manufactures, 1904, Part I, pp. cciv.

manufacturers, with a large part of the remainder in the States of New York, Pennsylvania, Illinois, and New Jersey.

The products of manufacture in this non-ferruginous industry are exceedingly varied and important, such as trinkets, fixtures, and ornaments of all kinds, plumbing, chandelier, bed, automobile, and soda-fountain parts, valves, couplings, nipples; white metal, German silver, gun-metal, bell-metal, type-metal, aluminum and all its alloys, solders, babbitt, pewter, railway car journals, etc.

CHICAGO BRASS MANUFACTURING. In the summer of 1910 there were 182 brass manufacturing concerns inspected in Chicago.[34] Of these 89 were found to be engaged in the brass foundry or refining business, representing in all 2212 employees within the foundries. These foundries were found to be located in all manner of places, from basements, midfloors, and top floors in great buildings to specially built foundry buildings.

It was found that skilled labor was employed in the small jobbing and specialty shops almost altogether, whereas the large concerns which were usually making standard type products, had machine moulds and employed large numbers of unskilled foreigners. Women were found to be employed only in core work, usually in small rooms more or less ineffectively partitioned off in one corner of the foundry room. Skilled laborers were found to be mostly Americans, Englishmen, Scandinavians, and Germans. The unskilled, who outnumbered the former by ten to one, were nearly all Polish or Bohemians; 12 of the 89 firms employed union labor only, most of the large concerns were strictly non-union, whereas the balance were said to be "open shop." It was found that the non-union concerns and many of the others were united together in an organization known as the Chicago Brass Manufacturers' Association, which maintained a central office, and had as a not unimportant duty the employing and approving of workmen.

The question of ventilation in these 89 foundries was carefully investigated. It was found that 45 were so situated that surrounding buildings interfered with whatever natural ventilation they had. That in only 6 were the furnaces located in a separate room from the moulding and casting quarters. Only 12 had a separate core room, whereas over one-fourth of the total firms had not provided separate quarters for processes strictly ulterior to foundry work. Practically everywhere only natural ventilation by means of roof apertures, windows, and doors was depended upon to free the foundry quarters from the noxious vapors of molten brass. Only 9 had made any attempt at artificial ventilation, such as suction fans, blow fans, etc. Adequate ventilation, especially as regards any sort of inclement weather, was found to exist in only 22 places, and in none of these could it be considered better than fair.

[34] Loc. cit.

Light was found to be good in 50, fair in 21, poor in 17, and artificial only in 1 foundry. Temperature was unduly hot in 25 foundries, whereas it was found that nearly one-half depended upon soft-coal stoves for general room temperature in the winter-time, and not a few upon open salamanders. In many places the general sanitary arrangements, such as facilities for washing, places for changing clothes, toilet rooms, etc., were either lacking or very inadequate, and usually fully exposed to the foundry vapors and fumes.

In no foundry was room space found to be less than 500 cubic feet per person. It is quite evident, however, that foundries should not have their cubic air space measured on the same basis as that of a living room or even a workshop room. The height of roof or ceiling was noted in each foundry, and showed that in 26 it was 12 feet or less. When such was the case with the absence of overhead ventilators the escape of brass fumes from furnaces and during pouring was greatly hampered. In only 2 places were special rooms provided as eating quarters, and it was found that the workmen almost invariably ate their lunches in the foundry room. In most places the first pouring had been completed just before the noon hour, hence the fumes and sublimation products were still in the atmosphere to a greater or less extent at that hour.

There was considerable complaint among many brass moulders of the constant physical and mental strain required at the present day. It was claimed that a foreman or other expert would set a pace on a certain class of work for a few hours or a day's time, after which the men were compelled to keep up to this record, or be docked on the day's pay. The hours of work in practically all places was found to be from 7 A.M. to 5.30 P.M., with a half-hour lunch period.

The amount of exposure to brass fumes varied considerably in different foundries and to some extent with different classes of workmen. In places where pouring was done but twice daily the exposure was minimal, but where it occurred from four to six times daily, each time requiring from ten to thirty minutes to clear the atmosphere, and in several large establishments where pouring was practically continuous all day, there was almost a constant exposure. In the latter places the workmen often sickened before the day was over and had to quit for the day. The winter season was bitterly complained of by many workmen, because of the necessity of closing the means of natural ventilation to prevent chilling of the moulds. As a rule, the furnacemen were the most exposed, and the greatest sufferers.

In places where refining of old scrap metal was done cases of chronic plumbism were occasionally encountered. Also it was found that in nearly all foundries from 0.5 to 7 per cent. of lead was contained in the alloy. Phosphorus was found to be in almost

universal use, but in limited quantities, and no diseases directly traceable thereto were found. In type foundries and refineries there seemed a liability to antimony poisoning, but no cases were discovered.

Other deleterious influences to which brass-founders were exposed were found to be carbon-monoxide gas from improperly ventilated furnaces, and the nauseating odors of burnt oil from oil-blast furnaces. Occasionally, where supplementary processes were carried on in the foundry quarters, the atmosphere was found contaminated with metallic dusts from polishing and buffing, with mineral acid and alkali vapors from cleansing processes and cyanide vapors from plating tanks.

Evidence of occupational disease was closely inquired into at all foundries, both from officials and workmen. There were a total of 114 officials consulted, representing 83 foundries. Of these officials 31 admitted the presence of occupational diseases in their own plants, 26 others gave interesting statements concerning the same, 46 declared no knowledge of the same, and 11 refused any comment. Of 187 workmen, 146 reported that they were subject to brass chills.

The forms of sickness most commonly complained of were:

Brass chills, 45 of the 89 foundries.

Smoke inhalations, 26 foundries (especially fumes from oil-blast furnaces).

Other acute sicknesses, 4 foundries.

Other chronic sicknesses, 20 foundries (respiratory, gastro-intestinal).

Temperature variations, 11 foundries.

Fatigue, 3 foundries.

Of the total of 2212 men and women in brass foundries it was found that 451 were engaged in processes which need not have exposed them to the foundry atmosphere. Of the remaining 1761 actually engaged in brass foundry work age statistics were carefully compiled with the following startling disclosures: 17 over fifty years of age, about 60 over forty-five years of age, and about 180 over forty years of age, leaving 1500, or 85 per cent., under forty years of age.

An investigation carried on into the zinc smelting industry in the Illinois River Valley where 3 concerns employed upward of 2000 men, disclosed the presence of the following industrial diseases and complaints: (1) "Zinc chills" which, from description by the workmen, were exactly analogous to the brass-foundryman's ague. However, this complaint was found to be of rather infrequent occurrence, as the smelters were found to be not as much exposed to the zinc smoke, as brass-moulders. (2) Lead poisoning, which was of greater frequency than among brass-moulders, because of the handling of crude ores. (3) Summer colics, which the work-

men alleged to be due to the drinking of ice-cold water when overheated, but which may have been the expression of a seasonal form of lead colic. (4) Respiratory afflictions, which existed with great frequency, and known among the men as "asthma," due to breathing zinc fumes. (5) Carbon-monoxide poisoning, among the gas-plant workers, as all of the concerns made their own gas, which was used for fuel in the smelters. (6) Industrial alcoholism, which I so name because the workmen consider alcoholic liquors antidotal to various forms of trade sickness.

Limitation and Prevention of Occupational Brass Poisoning. The chief means of preventing brass-founder's ague lie in the prophylaxis. This consists in proper hygienic arrangements in foundries and smelters, regulation of the habits of workmen, and large roomy quarters. All furnaces and furnace areas should be provided with hoods and stacks to draw off escaping vapors. In addition ceiling ventilators or skylights provided with artificial means, such as suction fans, or blower systems, to be used in inclement weather, should be provided in every furnace and foundry room. The furnace room should be separate from the balance of the foundry. In large foundries with good ventilation whether natural or artificial, brass chills practically never occur. The prevention of metallic fumes seems impracticable, although they can be largely absorbed by adding silicates, fluorides, and borate to the slag (Sigel). Adequate light, wet cleansing, and frequent whitewashing should be resorted to. In addition proper precautions as to lead poisoning in certain classes of work, as well as the prevention of the other unhygienic conditions mentioned, should be looked into.

Individual precautionary measures, such as sponges, respirators, etc., have a restricted value, but are generally little and reluctantly used. Sickly or anemic workmen, boys, and women, those with a tubercular tendency, and chronic alcoholics should not be employed in brass foundries. The workmen should not eat in foundry quarters where the air is filled with sublimation products; they should be allowed time for washing up before eating, and longer lunch periods. They should be given adequate washing facilities, and be provided with shower baths, and have suits at least of outer garments for use during work hours.

No specific treatment for brass chills has been discovered. The more careful and observing workmen use mild emetics, since they claim that the production of vomiting relieves the distressing symptoms at once, while a good purge seems as beneficial as anything. As before stated most of them resort to alcohol, usually whisky, but there is absolutely no proof that it has any beneficial effects. Many workmen seem to derive some benefit from drinking hot milk, to which they often add pepper. Sigel suggests that the workmen use sodium bicarbonate to form insoluble zinc carbo-

nate, but says that inasmuch as most (one-quarter part) of the metal finds its portal of entry by way of the respiratory system, this can do but very little good.

The State of Illinois has recently provided two laws for the effective prevention of occupational diseases, including brass poisoning, the enforcement of which lie with the Department of Factory Inspection. The first of these came in force January 1, 1910, and is entitled:

"An act to provide for the health, safety, and comfort of employees in factories, mercantile establishments, mills and workshops in this State, and to provide for the enforcement thereof."

The second came immediately following the Report of the Commission on Occupational Diseases to His Excellency Governor Charles S. Deneen, and has been enforced since July 1, 1911. It is entitled:

"An act to promote the public health, by protecting certain employees in this State from the dangers of occupational diseases, and providing for the enforcement thereof."

In certain parts of Germany, according to the statistics of Frey,[35] the enforcement of hygienic measures between the years 1901 and 1909 has already produced marked results in this industry.

SUMMARY. 1. In a broad sense the brass industry includes all non-ferruginous metal-working trades; zinc is invariably present to some extent; there are sixty or more common alloys (brass, bronze, German silver, type-metal, etc.). The proper physical properties are produced by combining with zinc varying proportions of other metals, as copper, tin, lead, nickel, antimony, phosphorus, etc.

2. Strictly speaking, brass is a compound of copper and zinc (lead, a trace to 7 per cent.). Bronze is a compound of copper and tin (some zinc, also lead).

3. There is no peculiar poisoning due to trauma from brass or the industrial exposure to brass dust, as among polishers, but greenish discolorations of the skin, hair, gums, etc., may occur, due entirely to the copper constituent.

4. Occupational brass poisoning or brass-founder's ague is a malaria-like complex of symptoms with certain limitations as regards occurrence, severity, susceptibility, and effects, found to occur chiefly among brass-founders, but also in all confined places where zinc is heated to the volatilization point and the resulting sublimation products inhaled.

5. This malaria-like symptom-complex is peculiar to the human being. As a rule, its severity is in proportion to the concentration of the zinc in the alloy.

[35] Vrtljschr. f. gerichtl. Med., Berlin, 1912, 3, F., xliii, 1. Suppl. Heft, S. 113–141.

6. There is no definite pathology, but continued exposure appears to be followed in time by chronic systemic affections (respiratory, digestive, urinary, and nervous). Zinc is found in the urine and feces.

7. The affection is very little known to physicians because it is never immediately fatal, its course is brief and self-limited and an apparent but fleeting immunity is soon established in most persons. The affection was first distinguished from malaria by Thackrah, in England, in 1830. The entire literature upon the subject to date is scarce.

8. The exact etiology is disputed. Long thought to be a copper poisoning, or an alloy poisoning, also due to other metals. Lehmann first produced the symptoms in man by burning chemically pure zinc. "Resorption of cell contents which have been destroyed or changed by zinc in the respiratory tract may be the cause of the peculiar malady."

9. Recent observations show it probable that the symptom-complex may be produced by the inhalation of the volatile products of other metals. The malady has always been associated with zinc, however, because zinc is the only supposedly innocent metal whose boiling point is commonly reached in the industries.

10. Recent perfections in the tests for zinc have enabled us to trace zinc through the lungs, liver, and kidneys of the rabbit exposed to the inhalation of brass fumes.

11. The hygienic and working conditions were investigated in 89 brass foundries and 3 large zinc smelters in Chicago and vicinity in 1910 by a State Commission, with the following findings:

(*a*) The large majority of these plants were without proper ventilation. Numbers of workers were also needlessly exposed to brass and zinc fumes.

(*b*) Workers invariably ate within the foundries, the noon hour was only thirty minutes, washing facilities were inadequate, the piece-work system prevailed (ten hours per day), and exposure to lead and its fumes, carbon-monoxide vapors and burnt oil odors were nearly universal conditions.

(*c*) Unskilled labor (Eastern Europeans) constituted 90 per cent. of the employees.

(*d*) Workmen were found in half the plants who were or had been the subjects of brass or zinc chills.

(*e*) About one-third of the officials consulted acknowledged the existence of these chills, but considered them of minor significance.

(*f*) Brass or zinc chills were far more prevalent in the winter season (natural means of ventilation curtailed).

(*g*) Large, well-ventilated plants or those provided with special means of artificial ventilation were seldom the site of the occurrence of these chills.

(*h*) Alcoholism was exceedingly prevalent, excited by chronic respiratory irritations. Undoubtedly the cause of much incapacitation. Traditionally antidotal to the effects of fumes.

(*i*) Trade-age-limit statistics showed: Only 17 out of 1761 men over fifty years of age and approximately 85 per cent. under forty years of age. Officials claimed workmen became too slow and undependable. Workmen claimed they were gradually incapacitated by the continued inhalation of fumes and vapors. Conditions not so among iron moulders, an analogous trade.

12. Prevention (no antidote or hardly a palliative for the zinc-chill syndrome): Restrict certain persons from the trade. Prevent the inhalation of metallic fumes as (*a*) by confining the fumes to certain quarters, (*b*) by insuring rapid ventilation, and (*c*) by coöperation on part of employees through instructions.

13. Following the report of the Commission the Illinois Legislature adopted a special occupational disease law effectively covering the hygiene of this and similar trades. By similar means, statistics show Germany has materially increased the trade-age-limit in this industry in recent years.

REVIEWS

THE PRINCIPLES AND PRACTICE OF OBSTETRICS. By JOSEPH B. DE LEE, A.M., M.D., Professor of Obstetrics at Northwestern University Medical School. Pp. 1028; 913 illustrations. Philadelphia: W. B. Saunders Company, 1913.

THIS text-book is a welcome addition to the field of obstetric literature. The author's twenty-one years of experience enable him to speak with authority, and the years of teaching he has spent are evident in the systematic and clear arrangement of many of the chapters. The greater part of the book is most excellent, especially the chapters on the mechanism of labor and on deformities of the pelvis. The reviewer knows of no text-book in which these two subjects are better handled. Most excellent also are the chapters on extra-uterine pregnancy; the diagnosis and differential diagnosis of pregnancy; and the greater part of the chapter on puerperal sepsis. The illustrations are superb, the publishers having exceeded even their high standard in this respect. Most noteworthy are the illustrations on the Porro Cesarean operation, and the full-page plate, Fig. 435, of Wegner's sign of fetal syphilis.

In a book of this kind, in spite of its many good points, there are a few examples of questionable teaching; some a matter of opinion only, but some diametrically opposed to modern teaching, and also quite a few omissions of matter that should have been included. It seems strange to meet in these days an endorsement of episiotomy, based as it is on an erroneous idea of the production of perineal tears; an endorsement of the use of the finger as a curette in abortion, instead of the placental forceps; a recommendation of the use of a 1 to 1500 solution of bichloride of mercury in the vagina in labor. The chapters on toxemia of pregnancy (especially the latter half of pregnancy) are not arranged with the same care that is bestowed upon many other chapters, and the discussion of the subject is involved.

While the text recommends the use of rubber gloves, a large proportion of the illustrations omit their use, especially Figs. 312 to 318, where the technique is not such as to inspire admiration. The method of filling a colpeurynter, shown on page 456, can hardly be compared to the use of a metal piston syringe for this purpose, as the Davidson syringe shown is notoriously hard to cleanse

and care for adequately. The prohibition of disinfection of the uterine cavity in septic abortion (p. 433) is justified only when the instruments used are employed with undue force. The spread of infection spoken of is due to poor technique and not to the proper employment of either curette or placental forceps.

There are some omissions of subjects, possibly not unusual in first editions. One looks in vain, for instance, for any mention of blood pressure in eclampsia; the pulmotor or mouth-to-mouth insufflation as a means of reviving an asphyxiated child; any description or mention of cystoscopy or catheterization of ureters; any mention of extraperitoneal Cesarean section; the more modern perineal operations for repair of the injuries of childbirth, based upon an accurate knowledge of the site and character of the injuries. The chapter on abnormalities of the newborn child might with advantage be made more comprehensive in future editions. Much too little is said of the consequences of childbirth, to be managed during the puerperium or shortly afterward; in this respect the book does not follow the proper course of safeguarding the patient's future comfort, but deals with the subject from the standpoint ofmidwifery rather than obstetrics.

These criticisms are mostly of a minor nature, however. The book is a valuable one, and worthy of a place of honor in any medical library.

The make-up of the book and particularly the illustrations are on the very highest plane. J. C. H.

A Text-book on the Practice of Gynecology. For Practitioners and Students. By W. Esterly Ashton, M.D., LL.D., Professor of Gynecology in the Medico-Chirurgical College of Philadelphia. Fifth edition. Pp. 1100; 1050 illustrations. Philadelphia and London: W. B. Saunders Company, 1912.

The general arrangement as well as the subject matter of this last edition differs but little from that of former editions so well known to the profession. Throughout, the book is characterized by minuteness of detail in both description and illustration which in the author's opinion, is essential to a book intended primarily for the general practitioner and student. While much can be said in favor of this plan, we believe that such efforts have been carried too far thus detracting from rather than contributing to the object in view. The student as well as the practitioner seeks essentials elaborated by detail only when the importance of the subject demands further elucidation. The schematic drawings

are as a whole good, but here again the idea of detail runs rampant and many illustrations could be omitted with benefit. For example, we cannot see the necessity of depicting the instruments required for each operation or such well-known articles as a glass rod, an alcohol lamp, a rubber glove, etc. This fault detracts from what is otherwise an excellent book, in which a large practical experience has been the guiding hand in presenting the modern views of gynecologic diagnosis and treatment. The various aspects of each disease are exhaustively discussed and the treatment advised is characterized by sound conservatism and good judgment. In this last edition such alterations and additions have been made as were necessary to bring the work up to date. The use of the *x*-rays in the treatment of uterine myomas is briefly mentioned and is recommended in only exceptional cases. Fulguration is advised as a routine treatment in operations for cancer and desiccation advocated in the treatment of warty growths of the vulva. Minor changes have been made in the chapter dealing with cystitis; cystoscopy is described but the entire chapter is antiquated and should be rewritten. The von Pirquet test is recommended in the diagnosis of tuberculosis; the more important focal reaction following the subcutaneous injection of tuberculin is not mentioned. Additions to pathology include actinomycosis, malignant leiomyoma, Krukenberg's tumor, pseudomucinous cystadenoma, and the investigations of Loeb concerning the etiology of dermoid cysts. The treatment of gonorrheal and septic infections of the uterus and tubes has been practically rewritten and conforms with the views now generally accepted. Changes in technique and operations include the use of iodine in the preparation of the field of operation, Baldy's suspension of the uterus, Ward's treatment of vesicovaginal fistula, salpingo-oöphorectomy and partial hysterectomy, and the author's recently adopted method of removing the appendix. F. E. K.

THE PARASITIC AMEBÆ OF MAN. By CHARLES F. CRAIG, M.D., Captain, Medical Corps, United States Army. Pp. 253; 30 illustrations. Philadelphia and London: J. B. Lippincott Company.

THE importance of the subject to the medical profession amply justifies the publication of Captain Craig's monograph as a presentation of an authoritative review of the information which has thus far been acquired of the amebæ parasitic in man with exposition of proved methods of study for their recognition and identification. The book includes chapters upon the history of this subdivi-

sion of microbiology, on the morphology and biology of amebæ in general, upon their classification, the technique of the study of parasitic species, the question of the possibility of their artificial cultivation, with systematic description of those parasitic forms to be met in the human intestinal tract, in the mouth, the genito-urinary tract, and in exudates, abscesses, and in the lungs.

It is true that the book might without loss be materially condensed, and suffers somewhat from unnecessary repetitions and diffuseness of the discussions; but at the same time it is written in an easy conversational style which cannot be without attraction for the reader, and the material presented and in general, the opinions stated are altogether commendable. The chapter on technique is a timely one and valuable to any medical man desiring to pursue study along the author's lines; and the descriptions of amebic parasites with the points emphasized for the study of the different species are reliable. Naturally differences of opinion exist in these matters as in most others, but the reviewer feels that Craig has been frank and fair in setting forth his position upon such moot points, as for example, the question whether the cultivation of pathogenic amebæ has actually been accomplished, as by Musgrave and Clegg, or whether the forms obtained in culture are not really independent types. Craig follows the usage of the best protozoölogists in his nomenclature; employing the generic name *entameba* proposed by Casagrandi and Barbagallo in 1897 for parasitic amebæ (*Annali d'Igenie Sperimentale*, vii, 103). However, in 1879 Leidy (*Proc. Acad. Nat. Sci.*, Philadelphia, xxxi, 204) proposed the generic name *endameba* for parasitic amebæ, dealing at the time with a parasitic ameba of the cockroach; and, therefore, by our modern rules of nomenclature the name should be spelled with a "d" instead of a "t," with attachment of Leidy's name instead of those of Casagrandi and Barbagallo when reference to the genus alone is made. The writer is in full accord with the author in questioning the validity of a number of species which have been proposed, as Endameba kartulisi, E. pulmonalis, E. nipponica, E. urogenitalis, and others. As a matter of personal interest he would have been pleased to have noted discussion by Captain Craig of the E. mortinatalium presented in 1910 by Smith and Weidman in minute abscesses in the kidneys and elsewhere in a stillborn infant. One misses in the work any reference to Leydenia gemmipara, Schaudinn, which because of its discovery in connection with cancer was for a time a matter of wide interest and is commonly included among the protozoan parasites of man; but he is technically correct in excluding it from the limitations set to the present volume since it is now known to be in reality only an amebiform stage of one of the Foramenifera, chlamidophrys stercorsa, Cienkowsky. Nevertheless, from a comparative standpoint, for purpose of enabling differentiation in case of occurrence,

it might well have been given appropriate space. Suggested by analogy, some question might be raised in the matter of classification in case of the author's Parameba hominis, fully and in the reviewer's opinion very properly presented. It should be remembered that Schaudinn's genus Parameba is by no means above doubt as to its precise relation, the amebic stage being succeeded by a flagellate form bearing two chromatophores in the type species P. eilhardi, Schaudinn. There is a chance that an ameba and a flagellate have here been confused; or perhaps the prominence in classification should be given rather to the flagellate phase than the amebic. These, however, are all matters which in no sense detract from the real value of Dr. Craig's book to medical men; and at best are for the most part open to personal interpretation. The volume is a valuable contribution to English-speaking medical men, and should be accorded warm appreciation.

A. J. S.

VORLESUNGEN ÜBER KLINISCHE HEMATOLOGIE. By DR. WILHELM TÜRK, Privatdozent für innere Medizin an der Universität in Wien. Part II, first half. Pp. 410. Vienna and Leipsig: Wilhelm Braumüller, 1912.

THE author explains in the preface that the reason for the delay in the appearance of this the second part of his "Vorlesungen" is largely due to the fact of his withdrawal from the Neusser clinic and the assumption of manifold new duties at the Kaiser Franz Joseph Hospital. In a certain sense this first half of the second part, in conjunction with Part I, should constitute Volume I of the entire book as it is planned. Part I covered much of the general pathology and anatomy of the blood, and in the present division of the work there are taken up particularly the physiology of blood formation, the biology and functions of the cellular elements of the blood, leukocytic reactions, including eosinophilia and the mast-cell reactions, inflammation, and variations in blood picture due to physiological conditions and alterations of environment.

There is in press a second half of the second part, which takes up the anemias and polycythemias, as well as the pathology of the erythroblastic apparatus; this is to be regarded as Volume II of the entire work.

The third part will cover the leukemias, the leukocytic reactions of infections, and the pathology of the leukoblastic apparatus. The plates for this volume are complete, but the text is not yet written.

The volume under discussion is an excellently arranged and

philosophical discussion of the various topics indicated above. Controversial matter is given brief consideration, and the writer's authoritative views given clearly and concisely. Embryology and morphology are considered in the usual way, but the work is made interesting by the discussion of the function of the various cells and cell groups under both normal and pathological conditions. If the reader seeks for immediately practical points in this book he will be disappointed, but if he seeks for enlightenment as to the broader significance of the function of blood cells and of their various changes in form and number he will be entertained and instructed by almost every paragraph. The book contains little that is original that has not appeared in monographs and other publications, but it is up to date in every particular.

H. T. K.

IMMUNITY. By JULIUS CITRON, M.D., Assistant at the University Clinic of Berlin, Medical Division. Translated from the German and edited by A. L. GARBAT, M.D., Assistant Pathologist, German Hospital, New York. Pp. 209, 27 illustrations, 2 colored plates, and 8 charts. Philadelphia: P. Blakiston's and Co., 1912.

GARBAT has presented with some additions an English translation of a work well known in Germany, the author of which, by reason of his extensive research and wide experience as a teacher, has treated his field with fulness and precision. Citron's manual on *Immunity* is at once a hand-book for the laboratory worker, and on account of its illuminating discussion of principles, a reference work for the clinician.

The book is so arranged that the physician even slightly familiar with the methods of the laboratory may learn the details of the various reactions and their significance. Methods which are used for diagnostic, therapeutic, and prophylactic purposes are discussed. There are also included fundamental considerations of immunity problems from a theoretical standpoint.

As a text-book, Citron's work is orderly and the text clear. The results of the various methods are presented critically. The beginning of the book is occupied with a discussion of the principles underlying immunity problems and a detailed description of laboratory technique. Then follows an account of active immunity with details of vaccination against small-pox, rabies, and typhoid fever. A large portion of the book is devoted to the important subjects of immunity against tuberculosis and syphilis, the account of the nature of the immunity acquired after tuberculin injections being of particular interest. It is rather astonishing to observe

that the author regards the ophthalmoreaction with so much favor.

The subjects of toxins, agglutinins, precipitins, bacteriolysins, and hemolysins are duly considered in accordance with the present state of knowledge regarding them. The discussion of toxins includes those derived from the higher plants and animals as well as from bacteria. The translator has somewhat revised the chapter on vaccines, and elaborated it to conform more closely to the most recently advocated views of Sir A. E. Wright. It is interesting to read that Wright does not insist so strongly as formerly on the determination of the opsonic index during vaccine treatment, and that Matthews, one of his assistants, states that in many cases, such determination is quite out of the question.

The consideration of immunity against the meningococcus seems brief, in view of the importance of the subject. Anaphylaxis too is little more than mentioned. The illustrations are adequate, the colored plates most excellent, and the experiments cited are accompanied by elaborate protocols. H. G. S.

DIAGNOSTIC METHODS. By RALPH W. WEBSTER, M.D., PH.D., Director of the Chicago Clinical Laboratory. Second Edition. Pp. 682; 37 Colored Plates and 164 Other Illustrations. Philadelphia: P. Blakiston's Son & Co., 1912.

THE second edition of Webster's *Diagnostic Methods* is an admirable hand-book for the laboratory, remarkable for its thoroughgoing character and conciseness. The selection of methods is wide and their description clear, the author emphasizing always the fact that laboratory results can be properly interpreted only in their relation to clinical phenomena. Much has been rewritten since the first edition, certain features eliminated, and many recent laboratory researches of proved value added. Among the latter may be noted the antiformin method for tubercle bacilli; Neubauer and Fischer's glycl-tryptophan reaction; Kendall and Day's method for isolating typhoid bacilli from the feces; Benedict and Bang's tests for glucose in urine; Wright and Kinnicut's method of counting the blood plates; Folin's newer methods for urinary sulphur compounds; the formalin method for ammonia in urine; colloidal nitrogen; the phenol sulphonephthalein test for functional activity of the kidneys; Noguchi's method for cultivating the spirochæta pallida; the tuberculin and luetin reactions; Noguchi's butyric acid test. The Wassermann reaction with its modifications is treated at length, and the section on serum pathology has been considerably enlarged. The book is well printed, of convenient size, and the numerous illustrations and plates are adequate. H. G. S.

COMPENDIUM OF DISEASES OF THE SKIN. By L. DUNCAN BULKLEY, A.M., M.D., Physician to the New York Skin and Cancer Hospital, etc. Fifth Edition, Pp. 286. New York, Paul B. Hoeber, 1912.

THE last edition of the writer's work appeared twelve years ago, and the present volume is of practically the same size and, with a few exceptions, of almost the same contents. The work consists of the subject matter contained in a course of lectures given by the writer at the New York Hospital. The rarer diseases have not been added, as the book is intended simply as an introduction to the subject of dermatology and for the general practitioner. Thirty thousand cases of diseases of the skin are reviewed by the writer, and there is also a therapeutic formulary. The work would be of greater value if more new material had been added, and if a certain remedy mentioned in the treatment of epithelioma, had been omitted. F. C. K.

PSYCHOLOGICAL MEDICINE. By MAURICE CRAIG, M.D. Second edition. Pp. 474; 17 plates. Philadelphia: P. Blakiston's Son & Co., 1912.

CRAIG in this book successfully attempts to treat the subject of insanity in a way particularly adapted to the teaching of students and general practitioners. His work contains considerable research of his own and many points of value and interest to an alienist. The author's lucidity and conciseness are most commendable.

The first part of the book takes up, in a manner as brief as clearness will permit, the study of normal psychology. Here sensation, affection, attention, conation, and other kindred subjects are considered.

The discussion of the term insanity and the etiology are next treated. The effect of metabolic changes is discussed, with the bacteriological and serological findings and conclusions of Bruce and others. Then, following a chapter on classification, comes symptomatology, a well-arranged and most useful section of the book. The diagnosis of beginning forms of insanity is here urged as most important, and the symptoms so often occurring as forerunners of insanity are taken up in considerable detail. Original investigations on blood pressure and metabolism are given with some of other authors.

In the chapters on mania and melancholia the so-called acute maniacal delirium described by Branchi and Piccinino is mentioned, and further original investigations are described. More than usual

stress is given to the danger of suicide in melancholia, a most important point which cannot be too strongly impressed.

The consideration of forms of stupor (anergic, post-melancholic, post-maniacal, catatonic), paranoia, and dementia præcox, is very thorough, and in the chapter on puerperal insanities an interesting opinion is given as to the probable effect of pressure upon the splanchnic vessels during pregnancy, causing high blood pressure and melancholia, whereas the fall in pressure after childbirth might account for the greater frequency of the maniacal outbreaks during this period.

Following the chapter on intoxication psychoses, paresis, the most important perhaps of all mental diseases, is discussed in a particularly thorough and detailed manner. Many original suggestions are advanced, among which is the author's belief that anti-syphilitic treatment is contraindicated in tabes and paresis, but that all measures should be used to reduce the possibility of cellular changes from exhaustion.

Dr. Craig emphasizes the impossibility of syphilis alone causing paresis, and he also suggests the possibility of the different types of paresis being dependent upon the type of brain tissue primarily involved.

Of the remaining chapters, all of which are written in accord with the standard of the earlier chapters, the ones dealing with epileptic insanity and feigned insanity and treatment are the most important, and corresponding weight is given to their discussion.

Throughout the work any points of medicolegal interest are clearly shown, and in a chapter devoted to the legal aspect of insanity, allowance must be made for the differences in the English and American codes. Many valuable plates (plain and colored), are given, including gross cortical changes and microscopic cellular degenerations in different diseases. E. M. W.

GYNECOLOGICAL NURSING. By ARTHUR E. GILES, M.D., B.Sc., F.R.C.S., M.R.C.P., Surgeon to the Chelsea Hospital for Women, Gynecologist to the Prince of Wales' General Hospital, Tottenham. Pp. 182; 41 illustrations. New York: William Wood & Co., 1912.

FROM cover to cover this little book contains a mine of information, couched in simple, readable diction. The introduction gives the author's conception of an ideal gynecological nurse, and it would be well for every nurse to learn it by heart as an important part of her stock in trade. The first three chapters are devoted to the anatomy, physiology, and diseases of the pelvic organs; the

author has selected the important points under each heading and describes them in such a manner as to make them thoroughly understandable. No detail is spared in the chapters dealing with the preparation for operation and the conduct of the nurse during the operation; every possible contingency is met, including the sterilization of instruments, suture materials and accessories, preparation of the room in hospital or private house, and the preparation of the patient before and during the operation. Post-operative treatment is likewise fully described, together with the commoner complications, their danger signals and treatment. The book is good throughout, and will prove of great value not only to the nurse for whom it is intended, but also to those who undertake the instruction of nurses in this branch of surgery. F. E. K.

THE PREVENTION OF DENTAL CARIES. By J. SIM WALLACE, D.Sc., M.D., L.D.S. Dental Surgeon and Lecturer on Dental Surgery and Pathology, London Hospital; Honorary Dental Surgeon to the West End Hospital for Nervous Diseases. Second edition. Pp. 70. London: Dental Record, 1912.

IN this small volume the author sums up his views of the etiology, pathology, and prevention of dental caries. He says that "the cause of dental caries is the prolonged retention or stagnation of fermentable carbohydrates in more or less immediate contact with the teeth and undisturbed by the free access of saliva." He claims that the only reliable method of preventing dental caries is the natural or physiological one, *i. e.*, self-cleansing of the mouth by foods that do not lodge between the teeth. In his opinion this is far more important than artificial procedures by tooth-brush, powders, and mouth washes, which have principally a cosmetic rather than a hygienic value.

If the book were read and its principles followed out by every physician, dentist, and layman having the care of children's teeth, the incidence of dental caries would be enormously reduced.

R. H. I.

SALBEN UND PASTEN MIT BESONDERER BERÜCKSICHTIGUNG DES MITIN. By DR. S. JESSNER, Sanitätsrat. Second edition; pp. 39. Würzburg: Curt Kabitzsch.

THE author first discusses the advantages and the disadvantages of the various salve bases, the absorptive properties, the ease with

which they may be applied, and the indications for the application of the same. Adipis, vaselin, paraffin ointment, vasogenum spissum, esypus, and casein ointment being among those mentioned. Casein ointment consists of cheese, water, and vaseline. Benzoated lard has the advantage over the plain lard of not becoming rancid. Various pastes are suggested as useful; chief stress is laid on the paste of Lassar, consisting of zinc oxide, starch, and vaseline, and Unna's paste, made of zinc oxide, terra silicea, and benzoated lard. The author has suggested the name "Mitin" for a base of his own composition which has an unusual faculty of absorption. The base consists of cold cream, resorbin, and eucerin. Resorbin consists of a fat, oil, and water; gelatin holding the ingredients together. Eucerin is a paraffin ointment. The base is of a thin or thicker consistency, depending upon the proportion of these substances combined. By combining powdered zinc oxide, starch, etc., to the base a white paste may be obtained. Various formulæ are given in the appendix showing drugs made up with Mitin as the base. F. C. K.

Carbonic-acid Snow as a Therapeutic Agent in the Treatment of the Diseases of the Skin. By R. Cranston Low, M.B., F.R.C.P.; Assistant Physician to the Skin Department, Royal Infirmary, Edinburgh. Pp. 117; 16 illustrations. New York: William Wood & Co..

Low has contributed a small volume which is not only of interest to the dermatologist, but also to all those practitioners of medicine who are interested in the newer therapeutic measures. The various methods for the collection and the moulding of the carbonic-acid snow are described in detail. The amount of pressure required and the duration of the application of the moulded snow are thoroughly and practically considered. A very interesting chapter gives the microscopic picture of the skin some hours and also some days after the application of the snow; the histological appearance explaining the action of the therapeutic agent. The results obtained in the treatment of numerous diseases of the skin are recounted. The most favorable response having been noted in nevus vascularis, nevus pigmentosus, and lupus erythematosus. The ninety-four references quoted make the volume of particular value to those using this method of treatment. F. C. K.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Treatment of Leukemia with Benzol.—A. v. KORÁNYI (*Berlin. klin. Woch.*, 1912, xlix, 1357) has tried benzol in the treatment of leukemia. He was led to do this by the results of experimental studies published by Selling, who showed that in animals poisoned with benzol, after a transitory rise, the leukocytes gradually decrease in number, and finally disappeared entirely from the blood, whereas the number of red blood cells underwent only a moderate decrease. Selling also observed a marked aplasia of the bone marrow, spleen, and lymphatic tissues in general. After withdrawal of the benzol, regeneration took place. Having a number of leukemics in the clinic, Korányi determined to use benzol in treating them. His experiences with it he summarizes as follows: (1) After a temporary increase in the number of white blood corpuscles, benzol causes a marked improvement in the leukemic blood picture. The decrease in number of the leukocytes begins usually at the end of the second or the beginning of the third week, proceeding slowly at first, then more rapidly. After a slight initial decrease, the number of the erythrocytes remains practically constant; after prolonged treatment, he has even noted an increase in the number of red cells. This sequence of events appears to occur in all forms of chronic leukemia. The spleen decreases in size, but the lymphatic glands are less influenced. The general condition of the patient improves much as it does with successful Röntgen treatment. (2) Benzol produces improvement less rapidly than the *x*-rays, but it may benefit a patient who fails to respond to the latter. Patients who have been treated previously with the *x*-rays seem to respond to benzol more promptly than others. The effect of the benzol

treatment is not lasting. (3) Small doses of benzol seem to stimulate leukopoiesis. Therefore, large doses are indicated in leukemia. Three to 4 grams of benzol daily may be borne for months. In certain cases Korányi has given 5 grams for short periods of time, but unpleasant effects, such as burning in the stomach, eructation, short attacks of tracheobronchitis, and vertigo, may follow. Gastric disturbances are usually lacking if equal quantities of oil are placed in the gelatine capsules with the benzol. If vertigo is complained of, the dose should be lessened. (4) Korányi has also used benzol in a patient with polycythemia and splenic tumor. The result was encouraging. At the end of the first week of benzol treatment, the number of erythrocytes rose from 9,000,000 to 10,000,000, but in the next three weeks it fell to 6,700,000. As the patient considered himself cured, he disappeared from observation. It will require more extended observations to determine the value of benzol in the treatment of leukemia and erythremia, but it seems worthy of thorough trial.

The Carbon Dioxide Tension in the Alveolar Air in Acute Febrile Disease.—L. S. Fredericia and O. Olsen (*Deutsch. Arch. f. klin. Med.*, 1912, cvii, 236) have investigated the carbon dioxide tension in the alveolar air in acute fevers. It has been shown that the carbon dioxide tension is lowered in conditions where the oxygen supply is lessened, after excessive bodily exertion, in cyanotic cardiac patients, in diabetics in coma or with untreated acidosis, and in uremia. The studies of Fredericia and Olsen show that in patients with acute febrile diseases the carbon dioxide tension of the alveolar air is also frequently lowered. They consider it possible that this is due to the mild acidosis which is frequently associated with febrile disorders.

A Test of Pancreatic Function.—R. Ehrmann (*Berlin. klin. Woch.*, 1912, xlix, 1363) describes a new, simple test of pancreatic function. It is based on the fact that neutral fat free from fatty acid is split only by pancreatic lipase; the resulting fatty acids are then converted into their green cupric salts. Commercial palmin has proved to be the most suitable neutral fat. Other fats, such as butter and oils, cannot be used. Emulsified fat in the form of milk or cream is also unsuitable, since it may be hydrolyzed by ferments other than pancreatic, although the butyric acid odor noted after removal of these foods from the stomach is due chiefly to the action of pancreatic enzyme. The patient takes the following test breakfast on the fasting stomach: About 30 grams of ordinary rice starch are dissolved in about one-fourth of a liter of water, and warmed somewhat. In this solution about 57 grams of palmin are stirred; the palmin is melted by warming. The mixture is drunk from a glass, and is allowed to remain in the stomach two to two and one-half hours, when it is removed. In testing the gastric contents, two solutions are required: Solution I, petroleum ether, 90, benzol to 100; Solution II, cupric acetate, 3, distilled water to 100. A portion of the fatty gastric contents is shaken vigorously with an equal quantity of solution I. The ether layer, after separation, is poured into a second test-tube, and is then shaken with an equal volume of solution II. The ether which again separates is stained more or less intensely emerald green, depending

upon the concentration of fatty acids in the gastric contents. With no hydrolysis of the palmin, the ether remains water clear. If the gastric contents are very acid (Congo paper turned a very dark blue), the reaction may be weak or may fail even with normal pancreatic secretion. In such case, repeat the test breakfast, adding to it a teaspoonful of sodium bicarbonate.

Contributions to the Pathology and Therapy of Very Severe Cases of Diabetes Mellitus.—R. GRAFE and CH. G. L. WOLF (*Deutsch. Arch. f. klin. Med.*, 1912, cvii, 201) have made complete metabolic studies of 3 very severe cases of diabetes mellitus. (The details of their studies cannot be adequately reviewed; the original must be consulted.) They have determined quantitatively the sugar, total nitrogen, acetone, β-oxybutyric acid, creatin, and creatinin, ammonia, "formol," and colloidal nitrogen, and have made observations upon the respiratory exchange of gases in the lungs. In 2 of the patients the acetone excreted was extraordinarily high. The dextrose-nitrogen ratio exceeded 5 over long periods of time, so that formation of sugar from fat must be assumed. They also found the respiratory quotient high in the same 2 patients. This apparent contradiction has also been found by other observers. From comparison of the analyses of the respiratory experiments and of the urine voided at the same time, Grafe and Wolf conclude that the dextrose-nitrogen value and the respiratory quoteint may be harmonized only if one assumes either that, twelve to eighteen hours after a rich carbohydrate meal, the severe diabetic possesses at least 20 grams of glycogen for oxidation or synthesis, or that a still unknown anomaly of metabolism is at play. Since there are no grounds to support the latter view, the first supposition is assumed to be correct. The relation of the creatin excretion furnishes a valuable index of the character of a case of diabetes; the more severe the case, the greater is the quantity of creatin excreted. Therapeutically, Grafe and Wolf found very large quantities of alcohol (equivalent to 100 to 160 grams of absolute alcohol daily), and large doses of alkali (sodium bicarbonate and sodium citrate, 70 to 100 grams daily for weeks) very useful. The beneficial effect of the alcohol was seen not only its action upon the acidosis, but also upon the sugar excretion.

A New Test for Diacetic Acid in the Urine.—B. V. ONDREJOVICH (*Deutsch. med. Woch.*, 1912, xxxviii, 1413) reports a modification of Lindemann's reaction for diacetic acid. Method: To 5 c.c. of urine add 5 drops of 50 per cent. acetic acid. To this mixture add a 0.2 per cent. methylene blue solution until the whole assumes a marked blue color; usually one drop suffices. Four drops of tincture of iodine are now placed in this mixture, on which the color changes to red. If diacetic acid is present, the blue or green color returns within one minute at the most; otherwise, the red color persists. The reaction depends upon the fact that in acid solution diacetic acid binds the free iodine, forming a colorless compound. Normal urine is supersaturated with free iodine after the addition of 4 drops of the tincture to 5 c.c. of urine; the excess of iodine unites with the methylene blue to form a red compound. An excess of acetic acid is to be avoided.

Ondrejovich finds the reaction twice as delicate as the Gerhardt test. If the urine contains so much diacetic acid that the reaction between it and iodine is instantaneous, the blue color remains unaltered. No substances have been encountered in the urine which interferes with the reaction.

Salvarsan in Chorea Minor.—J. SALINGER (*Münch. med. Woch.*, 1912, lix, 1376) adds another to the small list of cases of chorea minor which have been treated successfully with salvarsan. The patient, a girl, aged ten years, suffered from hereditary lues and chorea. The involuntary movements of the extremities were so violent that she was unable to write and frequently fell when attempting to walk; she constantly made grimaces. The Wassermann reaction was positive in the patient as well as in her father. Because of the lues, the patient was given 0.1 gram salvarsan intravenously. The same evening the involuntary movements had practically ceased. That the rapid improvement was not attributable to the more favorable surroundings of the hospital ward is probable from the fact that the patient, after a stay of two days, was discharged and remained well at home. In spite of the good results obtained in this case, in which lues also existed, Salinger believes that salvarsan should be used cautiously and not indiscriminately in chorea.

Scarlet Red in Artificially Produced Gastric Ulcer.—With the idea that scarlet red might have a beneficial effect in gastric ulcer similar to that observed following its use in the treatment of ulcers of the skin, DAVIS and DENNING (*Johns Hopkins Hosp. Bull.*, 1912, xxiii, 332) conducted a series of canine experiments studying the effect of the dye on artificially produced gastric ulcers. In a series of preliminary experiments they demonstrated the non-toxicity of the drug when taken internally, and noticed also that it had no purgative effect, nor did it affect the action of the kidneys. It was found, however, that the dye is a fat selecting vital strain being gradually eliminated in the course of months. Ulcers of varying depths were produced by means of a special punch. In one series of dogs the drug was given in 1 per cent. solution in olive oil in doses of 10 to 20 c.c., the total amount varying between 70 and 150 c.c. Five animals were thus treated and later sacrificed. Four showed more advanced healing of the ulcers than in the controls, and in the fifth both feeder and control were equally advanced toward healing. A second set of animals, fed with olive oil alone, revealed at autopsy ulcers which in 4 out of 5 cases showed less epithelial stimulation than in the corresponding experiments in which scarlet red olive oil was used. In these instances these ulcers were farther advanced toward healing than the controls, in one equally advanced, and in another less advanced sponding experiments in which scarlet red olive oil was used. In these instances these ulcers were farther advanced toward healing than the controls; in one equally advanced, and in another less advanced. In conclusion, Davis and Denning feel that the scarlet red solution caused a more rapid and better developed growth of epithelium in the group in which it was used than in the duplicate group in which olive oil alone was administered. The results with dry powder were not

favorable experimentally, but this may have been due to the fact that the material was not continuously in contact with the denuded area.

Eosinophiles in the Urine in Bronchial Asthma.—A. EDELMANN and L. KARPEL (*Deutsch. med. Woch.*, 1912, xxxviii, 1271) report their study of the urine of 4 patients suffering with bronchial asthma. In all of the patients there was noticed a slight cloudiness of the urine following the attacks of asthma, so that a cystitis was suspected at first, though there were no symptoms to suggest such a condition. The fresh specimen of sediment showed many leukocytes. Stained preparations revealed an eosinophilia of as much as 30 per cent. Careful examinations then showed that eosinophiles were always abundant in the urine following the asthmatic paroxysm. In none of the patients were there symptoms referable to the genito-urinary tract, and no epithelial cells or bacteria were found in the urine. There was no gonorrheal infection. The urinary changes consisted in the appearance of leukocytes alone; no other formed elements, such as casts or red blood cells, were found. The number of leukocytes resembled that seen in cystitis. There was no albuminuria. The cells make their appearance in the urine, as stated above, just after the paroxysm; during the dyspneic period the urine is clear or contains only an occasional leukocyte. The cells persist in the urine from a few hours to two days. Differential count of the cells of the urinary sediment showed 30 per cent. of eosinophiles in a patient whose blood contained only 8.5 per cent. of these cells. Edelmann and Karpel describe their methods of staining the cells of the sediment.

Lymphocytosis in Diabetes Mellitus.—L. CARO (*Berlin. klin. Woch.*, 1912, xlix, 1514), who called attention to the lymphocytosis of Basedow's disease in 1907, now reports the examination of the blood of 28 diabetics—a phase of the disease which has apparently been neglected heretofore. Practically all cases showed a reduction in the number of erythrocytes and in percentage of hemoglobin. The leukocytes were normal in number. Of the 28 cases, 22 exhibited a marked lymphocytosis; in 15 of the cases the lymphocytes varied between 40 and 70 per cent., while 7 cases showed less than 40 per cent. Only 6 patients had a normal percentage of lymphocytes (or a slight increase), but in these there were complications, such as suppuration, gangrene, tuberculosis, bronchiectasis. In 8 instances the eosinophiles were increased (up to 500 cells per cmm.). The lymphocytosis is independent of the severity of the disease and of the sugar content of the urine. No interpretation of the lymphocytosis is attempted. The thyroid gland is apparently not concerned in its production.

The Diagnostic Value of the Coin Sound in Pleuritic Effusions.—B. M. SLATOWERCHOWNIKOW (*Deutsch. med. Woch.*, 1912, xxxviii, 1282) has studied the *signe du sou*, described by Pitres in 1898, in 48 cases, 28 of which were exudative pleuritis. He finds that the most satisfactory method of eliciting the phenomenon is to have an assistant tap with one coin upon another which is placed over the dull area.

while the examiner auscultates the opposite side of the chest. If spongy or alveolar tissue intervenes between the points of percussion and auscultation, a dull tone without metallic quality is heard. With an air space (pneumothorax) the tone is, of course, intensely metallic. If a solid tissue or fluid is interposed between the points of percussion and auscultation, the sound is transmitted with an appreciable metallic quality. Heterogeneous tissue, as alveolar tissue and fluid, causes the sound to be simply dull. It is evident, therefore, that the distribution of the metallic sound in pleural effusion should correspond with the areas of dulness and diminished vocal fremitus. Slatower-chownikow finds, however, that the *signe du sou* extends 1 to 1.5 cm. beyond the lines marked out by percussion and vocal fremitus. With the exploratory needle he was able to demonstrate that fluid extended to the line given by the coin sound. He finds this method of examination very helpful in patients with weak voice. It is doubtless because of the difficulty of examining vocal fremitus in children that Pitres' observations have found their widest acceptance among pediatricians.

The Pathogenesis of Purpura Hæmorrhagica with Especial Reference to the Part Played by the Blood-platelets.—Duke (*Arch. Int. Med.*, 1912, x, 445) reëmphasizes the fact that in studying the various hemorrhagic diseases one must investigate all the various factors involved—bleeding time, coagulation time, platelet count, fibrinogen content, etc. The particular group of cases under consideration present a characteristic clinical picture: Purpura (petechia or ecchymoses), a tendency to bleed from every vascular lesion no matter how produced (prolonged bleeding time), normal coagulation time, a firm blood clot, and a clot which does not retract and exude serum. In milder cases the same essential condition may manifest itself only by ecchymosis, following slight injury, epistaxis, or hemorrhage due to local cause such as intestinal ulcers, esophageal varices, or profuse and prolonged menstruation. Coagulation time is always normal, the clot firm, retractility diminished. These conditions Duke believes to be due wholly or in part to the enormous reduction in the number of blood platelets which he found invariably present. In 7 severe cases showing the picture described above the number of platelets was reduced almost to the point of absence, all the counts being below 10,000, and as a rule below 1000 (normal, 200,000 to 400,000). In 6 milder cases they varied from 20,000 to 65,000. It was observed that the symptoms of the disease ran a course roughly parallel to the number of platelets, appearing when they fell to a very low level, and disappearing when the count rose. Furthermore, in 2 cases there was immediate relief following direct blood transfusion, and the relief being coincident with the increase in platelets following the transfusions. In both the clinical cases and in animals in which the platelet count was changed with subcutaneous injections of benzol, diphtheria toxin, and tuberculin, it was found that extreme symptoms of purpura hæmorrhagica only appeared when there were very low counts. Several counts of 40,000 to 75,000 were observed in patients who had no marked tendency to bleed, but no counts lower than these were observed in patients not subject to hemorrhage. Finally Duke points

out that this symptom complex may complicate various diseases, such as lymphatic leukemia, hemorrhagic smallpox, tuberculosis, nephritis, benzol poisoning, aplastic anemia, and diphtheria; the one feature in common being the low platelet count, and the resulting absence of contractility of the clot. Purpura hemorrhagica of the type described would seem, therefore, to be a symptom and not a disease.

Rhythmic Contraction of Heart-muscle Cells in Culture Media.—Using his adaptation of Harrison's cultural method, M. T. BURROWS (*Münch. med. Woch.*, 1912, lix, 1473) finds that the heart muscle cells of the chick embryo, after they have undergone division and differentiation without the organism, again assume their specific function both as isolated cells and as masses of cells. The rhythmic contraction of such cells corresponds to that of the heart of the living animal. The rhythmic movement was observed not only in the heart-muscle cells of young embryos, but also in the cells of embryos fourteen days old. Parts of the ventricle which are obtained from the older embryos do not themselves contract, although the isolated cells which have wandered out from such masses beat rhythmically. These observations furnish direct evidence in support of the myogenic theory of the heart beat.

SURGERY

UNDER THE CHARGE OF

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Tubercle Bacilli in the Circulating Blood in Surgical Tuberculosis.—KRABBEL (*Deut. Zeitschr. f. Chir.*, 1913, cxx, 370) examined 30 cases of surgical tuberculosis for the purpose of determining the value of the blood examination is differential diagnosis. Of 18 bone cases which were determined clinically to be surely tuberculous, the findings were positive in 12 or 66.6 per cent. Five cases of lymph node tuberculosis gave only one positive result, or 20 per cent. Four cases of skin, mucous membrane and tendon sheath tuberculosis, gave only one positive result, or 25 per cent. When we assume that a tuberculous infection of the lymph nodes is the result, in most cases, of a direct infection from the mucous membrane of the mouth or the tonsils, and as in skin diseases, it is a local process, it is easy to understand that the bacilli as a rule do not get into the blood. On the other hand, for the occurrence of a bone or joint tuberculosis, it is necessary for the

tuberculous material to first find its way into the circulation and then to be deposited at a site of lessened resistance. This explains why the tuberele bacilli can be found so frequently in these cases. The age of the patient and the duration of the process have little to do with the frequency with which the bacilli are found in the blood, and the finding of them has little to do with the question of the prognosis. The most important question that can be raised is as to whether the presence or absence of the bacilli can aid in the differential diagnosis. In one of Krabbel's cases the positive findings of the bacilli made the diagnosis certain before the histological examination of a specimen obtained at the operation furnished proof of the tuberculous nature of the condition. Krabbel believes that in cases in which there is not yet a clinically demonstrable lung tuberculosis, to point to a bacillemia, the positive findings of the bacilli can be of great importance in making the diagnosis certain.

A Contribution to the Anatomy and Pathology of Striped Muscle Fibers. Experimental Studies on the Theories Concerning Muscle Paralysis and Contracture.—KROH (*Deut. Zeitschr. f. Chir.*, 1913, cxx, 302 and 471) undertook an experimental study of ischemic muscle changes, being stimulated by the previous work of his chief, Bardenheuer, on the same condition. Ischemic contracture is a chronic condition resulting from connective tissue changes and consequent contraction. It is not due exclusively, as generally thought, to the direct influence of a transitory or long continued partial deprivation of oxygen and nourishment, nor is it due exclusively to the toxic effect of an overcharge with carbon dioxide. An important factor is the inactivity of the muscle, induced by the above mentioned directly damaging influences. The circulatory disturbances resulting from these begin and the inactivity completes the process of degenerative change. The circulatory disturbances may be due to a total interruption of the circulation for several hours by constriction of the limb or the occlusion of a large arterial trunk. In such cases a sufficient collateral circulation develops to prevent gangrene. Above all, the interstitial effusion of blood and lymph should be emphasized, since it increases the interstitial pressure. Substantial afferent and efferent branches may succumb to large interstitial effusions. Hemorrhage from very small vessels may lead to total compression of the largest arteries and veins. The efforts at expansion of small, otherwise unimportant interstitial effusions, may prove dangerous when resisted by some unyielding resistance. Thus a plaster of Paris cast may lead to most severe disturbances of the circulation, in some cases even to gangrene. The primary damaging influence of free effusions comes from the occlusion of smaller or larger arterial paths as well as from the suppression of the terminal collateral branches, not wounded but subject to venous pressure. The latter is especially worthy of attention because the retardation in the arterial capillaries interferes with the supply of oxygen and other nourishment and is combined with the direct toxic effect on the tissues which is most marked in the venous system from carbon dioxide. With inactivity the transforming strength of muscle movement is eliminated. In muscle movements are included the active and passive, and included among the latter are

massage, passive gymnastics, and electricity. They stimulate the circulation of the blood and lymph and may be a factor in the preservation of the extremity threatened by the stasis. The part played by the nerves in ischemic muscle contracture is difficult to determine.

Acute Gastric Ulcers Perforating into the Peritoneal Cavity.—WAGNER (*Deut. Zeitschr. f. Chir.*, 1913, cxx, 438) says that the only rational treatment for these cases is early operation. Operation within twelve hours gives a favorable prognosis, but after this time the prognosis becomes rapidly unfavorable. Since, however, cases with late peritonitis have been saved by operation, this becomes the last resort in late cases. As soon as a severe symptom is recognized, indicating an acute severe disease in the abdomen, as appendicitis, perforation of the intestine, gall-bladder, etc., the patient should be assigned to the surgeon. Only through early operation can the still frightful mortality be further reduced. By exact attention to the history and symptoms, among which the inital pain and muscle defence occupy first place, an exact diagnosis is possible in two-thirds of the cases. Morphine is to be avoided. Weakness is not a contraindication to immediate operation. The simplest, most quickly performed and, therefore, the most rational operation is the closure of the perforation by the Lembert suture, with or without freshening of the edges, and reinforcement by suturing over it a portion of the omentum. Gastro-enterostomy is indicated only in the presence of a pyloric obstruction or an hour-glass stomach. Excision or resection, as a rule, makes too great a demand upon the strength of the patient. If suture is impossible it may be replaced by covering the perforation by omentum or a gauze tampon. For the cleansing of the unclean peritoneal cavity, the best treatment is the sparing irrigations with warm physiological saline solution without unnecessary mechanical insult of the peritoneum. With less escape of the gastro-intestinal contents, a sponging out will be sufficient. Drainage with rubber tubes rarely does damage, but frequently prevents retention of secretions and abscess formation. In the after-treatment, the stomach should be spared by the copious administration of physiological salt solution, subcutaneously and by the rectum.

Subcutaneous Contusions of the Pancreas.—HAGEDORN (*Zentralbl. f. Chir.*, 1913, xl, 124) saw last summer, almost at the same time, 2 cases of subcutaneous contusions of the pancreas, in each of which operation was performed and the pancreas exposed. While much has been published on pancreatic diseases in recent years, little has been written of the injuries, especially of the isolated subcutaneous contusions of the pancreas. Both cases were very similar as to the kind of trauma at fault and the symptomatology, although one came to operation in the acute stage, the other later. In the first case three days before admission, the wheel of a heavy wagon passed over the upper part of the abdomen. The patient soon began to vomit and to be very ill and was taken to the hospital. The vomit was dark, the abdomen distended, tympanitic and slightly tender, pulse small and rapid, temperature normal, urine free of albumin and sugar, and there had been no passage of feces or flatus for several days. Gastric irrigations brought up considerable dark fluid contents, and some

relief followed, as indicated by no vomiting, the passage of flatus, a soft abdomen, and later passage of feces. This improvement continued for five days, when the severe symptoms set in again. Relief again followed gastric irrigations, which were repeated every few days. Then the patient gradually sank again and became of a grayish sallow color, emaciated, and apathetic. The temperature remained normal, but the pulse was 120 and small. Fourteen days after admission, a laparotomy showed an abundant bloody-serous fluid among the distended coils of intestine. The serosa was smooth and without adhesions. The omentum, mesentery, and fat appendages, were closely covered with numerous sulphur yellow, small nodules, and the mesenteric lymph nodes were swollen. The stomach and intestines showed no injuries. Two coils of small intestine were adherent to the pancreas by a brawny yellowish layer, about the size of a fifty-cent piece. Palpation could not detect any wound of the pancreas. Drainage was provided by tampon of the pancreas through the mesocolon, and the fluid was sponged from the abdomen. The wound was sutured about the drainage tampon. An abscess of the parotid developed later and was drained. Gradually recovery took place and eight weeks after the operation the patient left the hospital healed and strong. The second patient suffered the same accident as the first and showed very much the same symptoms. In the right lung there developed a dull area, laterally and below, and there was dulness in the lower abdomen. On the following day the patient showed marked collapse and was operated on immediately. The intestines were distended, the diaphragm was uninjured, but between the coils of intestine was some blood stained serous fluid. The serosa was smooth, but the omentum and mesentery were covered with typical sulphur yellow fat necroses. Exposure of the pancreas, to sight and palpation, showed that the pancreas was uninjured. The healing was without disturbance. There was no sugar in the urine, and eight days after the operation the patient was free of all disturbances. Sixteen days after the operation he was discharged.

Treatment of Total Rupture of the Urethra.—HOFMANN (*Zentralbl. f. Chir.*, 1913, xl, 155) in three cases of total, traumatic rupture of the urethra, did the following operation, after unsuccessful attempts at catheterization: After opening the bladder, a specially constructed metal catheter was passed through the internal orifice of the urethra to the site of the rupture. An incision was then made upon the beak of the instrument, exposing the latter. Now a partially flexible special catheter was mounted on the beak of the metal one and drawn out through the bladder and abdominal wall. The same metal catheter was then passed through the urethra from the meatus until it emerged at the site of the rupture, when the other end of the flexible catheter was grasped again in the same manner as before and was drawn outward through the urethra. The further care of the wound was conducted in the usual manner. The two ends of the soft catheter emerging from the bladder and urthra were tied together by a silk ligature. In this way the soft catheter could be drawn backward and forward daily, which contributes to the reëstablishment of the new bridge of mucus membrane. In the three cases operated on, soon after the removal of

the catheter, spontaneous urination was possible and the ruptured area healed without stricture. The only difference between the metal catheter and the usual one is that the beak is so formed that the channel of the catheter is continued from the side opening at the end in a groove to the tip, the end being conical. The end of the partially flexible catheter is small and so shaped that it fits into the groove in the beak of the metal catheter, and upon a pull on the latter both become locked together. Two figures illustrate these important alterations in the ends of the two instruments.

Chronic (Non-suppurative) Hemorrhagic Osteomyelitis.—BARRIE (*Annals of Surgery*, 1913, lvii, 244) says that the lesions in the ends of the long bones described as medullary giant-celled sarcoma, myelogenous giant-celled sarcoma, myeloma, and giant-celled tumor, should not be included in the classification of tumors. The process begins as the result of a trauma, and gives all the clinical and pathological evidence pertaining to a low grade inflammation. The foundation upon which the diagnosis of malignant tumor has been based is the presence in the tissues examined under the microscope of numerous gaint-cells which do not show any uniformity of architectural arrangement or boundary zones. It is an established fact that these giant-cells are not tissue builders, but scavengers, whose function is the removal of debris that is produced by low-grade inflammatory conditions occurring in bone. The whole process is explained on the basis of the lesion being due to a low-grade, ever present irritation or inflammation, which causes excessive production of vascular granulation tissue masses. From the clinical picture and the gross and microscopic pathology the condition presents, the term chronic (non-suppurative) hemorrhagic osteomyelitis seems a more correct definition of the lesion than the terms now in use.

Renal Tuberculosis in Children. Catheterization of the Ureters by Direct Vision.—ROCHER and FERRON (*Jour. d'Urolog*, 1913, iii, 153) report 6 cases in which catheterization by direct cystoscopy was employed with the patient under the affects of an anesthetic, local or general. The patient was placed in the Trendelenburg position and a urethroscope, No. 50, 7 cm. long, was introduced without great difficulty. The bladder was widely dilated with air. The mucosa was very red and presented ulcerations in the trigone on the left side. The orifice of the right ureter was normal while the left was replaced by a large black hole into which a No. 8 sound penetrated easily. Immediately about 10 c.c. of purulent urine escaped. The left kidney was removed. About two months later the patient had gained 3 kilograms in weight, was in good general condition, but the frequency of micturition persisted. They conclude that cystoscopy by direct vision is always possible, even easy, in a girl, aged over five years. The urethra admits easily a No. 40 tube, 7 cm. long, and notwithstanding the restricted field, the shortness of the tube permits the exploration of the bladder. In cases with a tolerant bladder, a mild Trendelenburg position suffices for the vesical distention, and this position is easily tolerated at this age. The bladder in the girl is analogous to that of the woman. While the interureteral band is often slightly marked,

it may be distinct. The ureteral orifice generally admits a No. 6 or 7 sound. In one of their patients, both ureteral meati admitted only a very fine bougie. This disposition does not depend on the age. They have encountered it in adults and all specialists have seen it. General anesthesia was frequently employed, not because the maneuvres were painful, but because very often the children were frightened by the instruments and became unmanageable.

The Abortive Treatment of Acute Gonorrhea.—LEBRETON (*Jour. d'Urolog.*, 1913, iii, 203) discusses the various substances and methods in use for the abortive treatment of gonorrhea and reviews extensively the French literature of the subject. By procedures of different kinds, limited or not to the anterior urethra, with the aid of very variable substances and doses, all the authors reviewed have obtained results that were often excellent and sometimes even remarkable. But there is no single method which is sure to give definite results. This is due to the fact that the disease does not always act in the same way, but its course varies according to factors which it is impossible to determine from the beginning. The results are sufficiently good to make it advisable to try the method whenever it can be done reasonably. It reduces the annoyances and complications which are always possible with an affection so tenacious and so dangerous as gonorrhea. The method to be selected from all those reviewed varies according to the particular case.

Clinical, Pathological, and Therapeutic Studies Concerning the Gastric Crises of Tabes Dorsalis.—CADE and LERICHE (*Deutsch. Zeitsch. f. Chir.*, 1913, cxxi, 41) discuss this subject at length, Cade from the medical side and Leriche from the surgical. In determining the method to be chosen and the procedure to be followed, when the indication for surgical interference arises in a tabetic patient, one should first attempt to recognize the nature of the crisis and to distinguish its chief elements. If the crises are very painful, with much vomiting, tachycardia, intermission of the pulse and laryngeal crises, one must fear a vagus involvement. The evidence of it should be sought and then the performance of a double-sided vagotomy, according to Exner, may be considered. This type of case, however, is the exception. Usually we have to deal with sympathetic crises. In these, we should proceed from the simplest methods of treatment to the most complicated operations. The most benign treatment should be tried first and the most severe reserved as the last resort. The simplest is that of König, who injects into the muscles of the back, on both sides of the spinous processes, 100 c.c. of a 0.5 per cent. solution of novokain. A lasting effect can probably be produced by the substitution of alcohol for the novokain and thus we treat the gastric crises as we do a facial neuralgia. If this method fails, Franke's operation may be tried. The fifth to the seventh intercostal nerves are excised (the number is determined by the result of the combined gastro-intestinal symptoms). After this, one may try the Jaboulay operation, that is, the stretching of the solar plexus. Should this method fail or be followed by recurrences, recourse may be had to the Foerster operation, seven roots on both sides being divided, if possible. If the

patient is capable of the necessary resistance and the crises are very severe, with a considerable participation of the intestines, the immediate division of the spinal roots should be undertaken. It would be very surprising if one did not succeed with one of these procedures, in giving these patients relief from their severe distress.

A Contribution to the Serum Diagnosis of Malignant Tumors.—Brüggemann (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxv, 877) calls attention to the interest shown in recent years in the serum diagnosis of malignant tumors. Although a series of reactions have been suggested for the diagnosis of the tumors from the blood stream and many authors have made investigations, the results are not yet satisfactory. In his investigations. Brüggemann employed chiefly the hemolytic test of Kelling and the meiostagmin reaction of Ascoli, although in a small part of the patients the Wassermann reaction was tried. Kelling found that in 66 per cent. of the patients with malignant tumors of the digestive tract, the serum produced a considerably stronger and more rapid hemolytic effect on the red blood corpuscles of hens, than the serum of patients with other diseases or healthy patients. With his test he was able in many cases, in which no tumor could be felt, to make a correct diagnosis as was demonstrated by later operation. Kelling designated his tests as IIa, IIb, and III. The IIa test determines the amount of hemolytic ferment in the serum, which is increased in malignant tumors. The IIb test shows the existence, according to Kelling, of a specific immunizing body combined with the red blood corpuscles of the hen. The III test shows that a certain amount of the specific immunizing body becomes, through inactivation for the red blood corpuscles of the hen, incapable of combination. Brüggemann employed Kelling's tests on the sera of 159 patients and on the sera of 16 pregnant women. He found that the tests IIa and IIb were not useful for the diagnosis of malignant tumors in general. In malignant gastric tumors, in the diagnosis of which Kelling specially advised the tests, the results were strikingly more frequently positive (68 per cent. of the cases) than with other gastric diseases (only in 7 per cent., or in 3.5 per cent. if those cases which had fever a short time before were excluded). This high percentage of positive reactions in malignant gastric tumors is particularly due, in Brüggemann's opinion, to the fact that marked destruction of the cancer, as it is seen in the stomach and intestines as well as in the ulcerated cancers of the mamma and uterus, causes a marked hemolytic effect in contrast to nonulcerated malignant tumors. A markedly positive result with test IIa in the case of an abdominal tumor, taken with other symptoms, supports the diagnosis that the tumor is in the gastro-intestinal canal or has invaded the canal. The test III gave irregular results although the number of cases investigated are admitted to be small. In a part of the positive results with the tests IIa and IIb, the weak reactions were probably due to the increased quantity of the normally occurring nonspecific hemolysins, in another part of the cases to the destructive products of the malignant tumors, which cause a strong hemolysis. The pregnant women showed a striking frequency of weak positive reactions. The meiostagmin reaction of Ascoli does not give a specific reaction for malignant tumors,

although one cannot deny that it has clinical value. Cachectic conditions not due to malignant tumors always gave a negative reaction. It can be an aid in the diagnosis of malignant tumors and will probably be generally adopted when the technique is made more simple.

THERAPEUTICS

UNDER THE CHARGE OF

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A New Cathartic for Subcutaneous and Intramuscular Administration.—CREDÉ (*Münch. med. Woch.*, 1912, lix, 2868) writes concerning sennatin which he isolated as the active principle of senna. He reports excellent results from its use subcutaneously or intramuscularly. He tried it in 300 cases and found it produced a bowel movement in about 83 per cent. of the cases. He advises its use in peritonitis and ileus, also as a prophylactic measure against postoperative intestinal paralysis. The remedy appears to have no toxic effects and produces pratically no local reaction when given intramuscularly.

The Value of Pertussis Vaccine.—SCOTT (*New York Med. Jour.*, 1913, xcvii, 176) reports 17 cases of pertussis treated with vaccines. Most of the cases were cured and in all the remaining cases the symptoms were distinctly improved. The number of attacks became less, their severity was diminished, cyanosis was less marked or vomiting during the paroxysms ceased. Children slept better, mainly because the attacks at night were less marked. The author advises an initial dose of 40,000,000 bacteria and gives the following doses with reference to the effects following the last dose. If much benefit arises he prolongs the intervals between the injections; if little or no benefit, he shortens them. He says that his experience seems to indicate that larger doses of vaccine should be given in the earlier stages of the disease. He also believes that infants require relatively higher dosage but fewer injections than do older children. The injections did not produce any local reactions. Scott believes that it is better to give a dose of 40,000,000 at short intervals for the treatment of severe cases rather than larger doses not so frequently repeated.

The Emetic Action of the Digitalis Bodies.—EGGLESTON and HATCHER (*Jour. Amer. Med. Assoc.*, 1913, lx, 499) say that the opinion is well-nigh universally held by clinicians and pharmacologists that the nausea and vomiting which sometimes follow therapeutic doses of the digitalis bodies are due to their direct irritant action on the gastric mucous membrane. Analysis of the literature shows that this opinion is based on deductions, and not on experimental evidence

obtained with therapeutic doses. This is wholly apart from the recognized fact that massive doses of these bodies applied directly to the gastric mucous membrane do cause irritation. The authors' experimental work on animals showed that all of the digitalis bodies caused nausea and vomiting when moderate doses were introduced into the circulation. They explained this action by a direct effect on the vomiting centre of the medulla and it was also found that vastly larger doses of some of these drugs could be introduced into the stomach without causing nausea or vomiting, and in such cases it was subsequently shown that little absorption into the blood stream had taken place. They believe that we have no means at present of securing the cardiac actions of the digitatis bodies without subjecting the vomiting centre to the influence of these agents at the same time, and there is no advantage in substituting one mode of administration; or one member of the group, for another, and the employment of opium to prevent the gastro-intestinal symptoms of the digitatis bodies in ordinary cases masks the appearance of toxic symptom which should serve as a signal for the reduction of the dose. The authors state that their results certainly lend no support whatever to the claims made that digalen, digipuratum, digitalysatum or the fat-free tincture of digitalis are in any way less actively nauseant or emetic in proportion to their cardiac activity than any of the better known and less expensive galenical preparations of digitalis and strophanthus.

Benzol in the Treatment of Leukemia.—BILLINGS (*Jour. Amer. Med. Assoc.*, 1913, lx, 495) reports 5 cases of leukemia treated with benzol. Four of these patients suffered from myeloid leukemia and one from a rather atypical type of lymphoid leukemia. All but one of the patients had received *x*-ray treatment before the benzol was begun. Röntgenotherapy was used in connection with the benzol treatment with all of the patients except in one patient where a severe *x*-ray burn prevented its use. Billings reports the cases in detail and a brief summary of his results in the individual cases is of great interest. The first patient had shown phenomenal improvement under *x*-ray treatment but had relapsed, and a severe *x*-ray burn necessitated the withdrawal of this method of treatment. At the beginning of the benzol treatment he had approximately 200,000 leukocytes, with a rather large percentage of myelocytes. Under the use of the benzol, the leukocytes melted away and three weeks after the drug had been withdrawn the fall continued and reached the low count of 3,600, with no myelocytes. With the great drop in the whites, the red cells amounted to about 5,000,000, and the hemoglobin from 85 to 90 per cent., so that while there was a destruction and removal from the peripheral circulation of the leukocytes, both reds and hemoglobin improved. There was a corresponding improvement in the patient's general condition; a gain in weight of 5 pounds, a feeling of well-being and lessened nervousness especially of the tremor from which he had suffered during his whole illness. The second and third cases require no special mention except for the fact that both patients had *x*-ray treatment for months with progressive improvement in the blood picture and also that there was diminution in size of the spleen; but

this improvement was slow and finally came to a stand. Under the use of both *x*-rays and of benzol the improvement became much more rapid, with corresponding improvement in general health. The fourth case deserves special mention because of the remarkable effect of the treatment. The patient had had two or three *x*-ray treatments before the benzol was begun on November 13. The first effect which was produced within six days, was to increase the number of leukocytes from 546,000 to 780,000. Three days later the count had fallen to 600,000; December 2, to 290,000; December 17 to 16,000, and January 5, the last examination, to 8,500. In less than two months of Röntgenotherapy and benzol treatment, the blood picture had returned almost to normal, and the myelocytes, which were found in the blood in a high percentage disappeared. The spleen, which was very large in the beginning, was just palpable on the last date. There was a corresponding general improvement in the patient's condition. In the fifth case the blood picture was that of lymphoid leukemia, but the lymph nodes were not large. The spleen was very large. With *x*-rays and benzol treatment the leukocyte count of 45,000 dropped to 19,000 in three days, then to 5,600 in six days. The benzol was continued experimentally, and January 5, about one month after beginning the treatment, the blood count was: hemoglobin, 68 per cent.; reds, 4,120,000; leukocytes, 5,900, of which there were small lymphocytes 35 per cent., large lymphocytes 9 per cent. and polynuclears 56 per cent. During the treatment the red cells and hemoglobin remained the same as at the beginning. The spleen rapidly diminished to not more than one-fourth the original bulk, and the small lymph-nodes disappeared. There was a marked improvement in the general condition of the patient. The benzol was usually given in gelatin capsules filled at the time of administration. One patient took the drug in an emulsion, made up by the hospital druggist, of which two teaspoonfuls equalled 15 minims of benzol. The drug was given soon after meals and at bed time. The beginning was 7 minims, which was soon increased to 15 minims. All patients complained of eructation of gas tasting and smelling of benzol. Burning in the stomach was a common symptom. As a rule the appetite was not disturbed, with one exception, and in this patient the general mitrition remained good. Of the other four all gained in weight. No other medicine was given except the necessary laxative or occasionally the mixture of rhubarb and soda as a stomachic. As a rule the patients were kept at rest. The benzol used was that obtained by the hospital druggist, and no analysis was made of it for the presence of nitrobenzol or anilin. However, Billings advises the use of a purified benzol on the ground of Selling's statement that impure benzol contains nitrobenzol and other products (anilin, etc.), and that anilin is the probable toxic substance producing purpura hemorrhagica, aplastic anemia, etc.

Antityphoid Vaccination in Children.—Russell (*Jour. Amer. Med. Assoc.*, 1913, lx, 344) says that the prophylactic use of antityphoid vaccine among children has, as yet, received scant attention in medical literature. He believes that this measure is highly desirable for children from two to sixteen years of age, who leave home for

summer vacations, schools, and colleges. Russell gives statistics based on the records of the inoculation of 359 children, between the ages of two and sixteen years, who have been vaccinated by fifty different physicians in many parts of the United States. The dosage is based altogether on body weight and not on age; the child is given that portion of the adult dose which his weight bears to the average adult weight, 150 pounds. If the fraction proves inconveient a little more, rather than less, is administered. As with adults the best time for inoculation is 4 o'clock, or later, in the afternoon, since any reaction will then come after bedtime. No harmful effects have been reported in any of the 359 children and, so far as known, none has contracted typhoid fever, although some of the vaccinations were made over three years ago. Revaccination in children should be undertaken earlier and oftener than in adults, since children are immunized on a basis of body weight, and consequently should be given a second course of two or three doses when the weight shows a very material increase. In the absence of final information as to the duration of the immunity it is probably advisable to revaccinate at least every three years in every case. Further experience may show that longer intervals are permissible.

Syphilitic Aortitis: Its Diagnosis and Treatment.—Longcope (*Arch. of Int. Med.*, 1913, xi, 14) reviews the literature concerning syphilitic aortitis and gives his personal observations regarding 63 cases in which syphilitic aortitis was proved to exist at autopsy or in which the diagnosis seemed reasonably sure from the combination of certain symptoms and signs with a positive Wassermann reaction during life. His conclusions are that syphilis produces a characteristic lesion of the aorta, which is responsible, as shown by autopsy statistics and the Wassermann reaction, for most aneurysms, about 75 per cent. of cases of aortic insufficiency in adults, many cases of dilatation of the aorta, and a certain group of cases of angina pectoris. The infection of the aorta probably takes place during the secondary stage and though the symptoms and signs of syphilitic aortitis with the complications may develop within a few months of infection, the process usually remains latent or unrecognized for an average of sixteen to seventeen years. Thus syphilitic aortitis is probably a common cause for the presence of a positive Wassermann reaction in so-called latent syphitis. The early symptoms and signs of syphilitic aortitis are a positive Wassermann reaction, precordial pain, slight dyspnea, attacks of paroxysmal dyspnea and angina pectoris, cardiac hypertrophy, increased pulsation of the vessels of the neck, and signs of dilatation of the aorta. Of the entire number of cases reported 20 were treated with salvarsan. Longcope says that the precordial pain, paroxysmal dyspnea, and angina pectoris are temporarily or permanently relieved by repeated injections of salvarsan, but in certain instances these symptoms, especially after large doses, may be aggravated for the first forty-eight hours after injection. The permanent relief of these symptoms can only be obtained, if at all. by the most persistent treatment. It is probably difficult to reach the spirochetes by the blood stream so that the diseased aorta is hard to attack. Longcope is impressed with the necessity of giving repeated

doses of salvarsan and with this method recurrences are not as frequent as formerly. He thinks that possibly neosalvarsan may prove more efficacious, or the combination of salvarsan with injections of mercury. The article is a valuable contribution to the subject and includes details of the cases observed by Loncope with a summary of the pathological changes of the disease.

Epidural Injections in the Treatment of Sciatica.—LANGBEIN (*Deutsch. med. Woch.*, 1913, xxxix, 20) reports 12 cases of sciatica treated in the last two years by epidural injections of novocain. Seven of these patients were permanently cured. Syphilis was a factor in one case that resisted the treatment. One patient improved temporarily but Langbein thinks that the trouble in this case was muscular rheumatism. He attributes the lack of improvement in 2 other cases to a probable exaggeration of their symptoms. Langbein gives the technique of epidural injections as practised by him in detail. One gram of novocain, $\frac{1}{4}$ of a gram of sodium bicarbonate and $\frac{1}{2}$ gram of sodium chloride are dissolved in 100 c.c. of cold distilled water. This mixture is injected into the sacral notch between the tubercles. In fifteen or twenty minutes after the injections all symptoms of the sciatica disappeared but he left the patients in bed for a few days. He advises the use of these epidural injections for cases of sciatica that fail to benefit after two weeks' treatment by the usual antirheumatic remedies.

PEDIATRICS

UNDER THE CHARGE OF

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Addison's Disease in a Boy, Aged Ten Years.—FREDERICK LANGMEAD (*Lancet*, 1913, clxxxiv, 449) reports a case of Addison's disease in a boy, aged ten years. The reported cases of this disease in children show that the general symptoms are similar to those in adults, although in children the greater number of cases run a very acute course, the pigmentation is less obvious, and death from coma and convulsions occurs more frequently. The present case lived but four hours after admission to the hospital. Pigmentation had begun about one year before, and attacks of diarrhea with increasing weakness had followed. The boy's father, two aunts and an uncle died of tuberculosis. The symptoms of the last attack were abrupt vomiting, restlessness, unconsciousness, flexed elbows, wrists and knees, subnormal temperature, and frequent convulsive seizures. The diagnoses of meningitis, uremia, and cyclic vomiting were entertained, but were ruled out by clinical findings, and no definite diagnosis was formed. Autopsy showed slight, general pigmentation with maculæ. The suprarenal glands were fibrocaseous throughout. Caseous foci were found in the portal fissure and the lowest lobes of the lungs. Microscopically,

giant-cells and tubercle-bacilli were found. The thymus, tonsils, the lymphatic particles of the tongue and intestines and mesenteric glands were hyperplastic. The heart weighed only 3 ounces, the small size being, no doubt, due to the accompanying weakness and the low blood pressure.

A New Disease-picture in Spasmophylic Diathesis.—RICHARD LEDERER (*Wien. klin. Woch.*, 1913, xxvi, 286) describes a hitherto unreported symptom-picture in children with spasmophilic diathesis. The respiration became very slow, difficult, and harsh. The dyspnea was usually expiratory and accompanied by a high grade of cyanosis. The spasmophilic attacks were usually acute, severe, and fatal, especially so in cases of laryngospasm or convulsions. Areas of impaired resonance with bronchial breathing and frequently rales were found throughout the lungs. The cases showing rales always showed a temperature of 38° to 39° C. and the condition in these cases was thought to be a pneumonia. On autopsy, however, there appeared absolutley no signs of a pneumonia. On the other hand, large areas of atalectasis were present, running deeply into the lung, and the intervening lung-tissue was emphysematous. Up to this time nothing was known of the spasmophilic action upon bronchial, smooth muscle. In these cases it was found there was a spasm of the small bronchial muscles, the lumen of the tube was shut off, and the alveoli were isolated from the external air, thereby becoming atalectatic. The rales were produced by local edema and transudation, due to circulatory stasis similar to the edema accompanying other spasmophilic manifestations.

Multiple Calcification in the Subcutaneous Tissue.—F. PARKSE WEBER (*British Jour. Child. Dis.*, 1913, x, 97) reports a case of "calcinoses" in a girl, aged seven years. There were a large number of hard nodules in the subcutaneous tissue of the extremities and adjoining parts of the trunk. The lymphatic glands of the groin, axilla, and neck were moderately enlarged. The nodules gave no pain or tenderness, except where the skin over them was adherent or ulcerated. The blood and urine were negative. The calcium index of the blood was 1.36, the normal average being 0.9. The duration of the nodules had been one year. During the preceeding year and a half the child had successively scarlet fever, diphtheria with paresis of the legs, pneumonia, abscesses of the axilla and neck, corneal ulcer, and otorrhea. The nodules were composed of calcium carbonate and calcium phosphate imbedded in a spongy framework of connective tissue. No uric acid or tubercle bacilli were found. The Wassermann and von Pirquet reactions were negative and the muscles and bones of the body were not affected. The condition seems to be similar to that found in scleroderma with subcutaneous calcification.

Antityphoid Vaccination in Children.—FREDERICK F. RUSSELL (*Jour. Amer. Med. Assoc.*, 1913, lx, 344) refers to the prophylactic use of antityphoid vaccine in children, and presents statistics based on 359 cases, aged between two and sixteen years, vaccinated by fifty different physicians in the United States. Russel believes it

highly desirable that all children aged from two to sixteen years who leave home for summer vacations, schools, and colleges be protected by this method. The local reaction to the injection is rather less than in adults. The general reaction is divided into four classes, based on the temperature: Class I, reactions absent; Class 2, mild, with temperature 100°; Class 3, moderate, with temperature 103°; Class 4, severe with temperature 103°. The dosage is based on body weight, not on age. The child is given that portion of the adult dose which his weight bears to the average adult weight, 150 pounds. The best time for inoculation is four o'clock or later in the afternoon. No harmful effects have been reported in any of the 359 children, and so far as known, none has contracted typhoid fever. Revaccination should be undertaken earlier and oftener in children than in adults, and a second course of several doses be given when the weight materially increases. At present revaccination is done after three years. This vaccine promises the greatest usefulness in protecting the younger ages, the most susceptible element of the population, from infection. A large proportion of the deaths from typhoid in this class can be prevented by antityphoid vaccination.

Infantile Scurvy Resembling Acute Articular Rheumatism.—Louis Fischer (*Jour. Amer. Med. Assoc.*, 1913, lx, 279) calls attention to the development of scurvy from canned foods in which the anti-scorbutic factor is wanting. No infant fed on breast milk acquires scurvy. Cow's milk must be fed in such a manner that it is not deprived of its enzymes. Boiling or prolonged steaming devitalizes milk and tends to develop scurvy. Fischer reports the case of a thirteen months' child who suddenly refused to stand. The slightest handling of the joints of the arms and legs gave severe pain and a diagnosis of articular rheumatism had been made. There was marked tenderness over the joints. The gums were soft and tender and had a bluish-red ridge around the teeth. The child weighed twelve and one-half pounds when aged thirteen months. There was a marked rachitic rosary. The infant was bottle-fed from birth, receiving condensed milk for one month and malted milk for seven months. The etiologic factor was the absence of fresh, live food, and the diagnosis of scurvy with rickets was warranted. The treatment consists in giving orange juice, pineapple juice, and expressed beef juice, raw white of eggs and very small doses of olive or cod-liver oil if the child can assimilate them.

OBSTETRICS

UNDER THE CHARGE OF

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The Prevention of Ophthalmia Neonatorum.—Von Herff (*Archiv f. Gynäk.*, 1912, Band xcviii, Heft 1) draws attention to the value of sophol as a prophylactic against ophthalmia. This substance in solu-

tion contains 18.5 per cent. of silver, and in over-saturated solution, 19.7 per cent. Tablets containing 25 centigrams are added to cold water to make a 5 per cent. solution. The tablets dissolve very slowly, but nothing should be added to make them dissolve, and the solution should not be warmed. It is used in the eyes as solutions of nitrate of silver are commonly employed.

The Treatment of Eclampsia.—FREUND (*Archiv f. Gynäk.*, 1912, Band xcvii, Heft 3) states his conclusions from the treatment of 551 cases of eclampsia in Franz's clinic in Berlin. He believes that, as we do not know the cause of the disorder, we must in a great measure use palliative treatment. He is in favor of the prompt and rapid emptying of the uterus in the interests of mother and child. There is need of a study of statistics as to the conditions and results between the first convulsion and the complete termination of labor. After the uterus has been emptied the condition of the kidneys and other eliminating organs must be carefully ascertained, and treatment instituted accordingly. In postpartum eclampsia when the pulse is hard and the tension high, bleeding is of especial value.

Rupture of the Uterus through the Scar of a Previous Cesarean Section.—JOLLY (*Archiv f. Gynäk.*, 1912, Band xcvii, Heft 2) reports the case of a rachitic patient who had a Cesarean section with a uterine incision 12 cm. long in the posterior wall, with the delivery of a healthy child weighing seven pounds. The uterus was closed with catgut. During the first eight days the patient suffered from fever, which at one time reached 104°. Mother and child were discharged from the hospital on the twenty-second day after the operation. Six months later pregnancy again occurred, and it was determined to perform Cesarean section with sterilization. The patient entered the hospital and labor began with vigorous pains. The os admitted two fingers, the membranes were unbroken, and the pulsating umbilical cord could be felt through the membranes. The patient was prepared for operation. When disinfecting the abdominal wall it was observed to be uneven and considerably tense. On examination the fetal parts could be felt directly beneath the abdominal wall. Apparently the uterus had ruptured during the patient's transfer from the hospital ward to the operating room. The abdomen was immediately opened, when the child and placenta were found free in the abdominal cavity. The child was delivered viable and living, weighing seven and one-half pounds. The uterus had ruptured through the old scar. As the patient desired sterilization, supravaginal hysterectomy was performed, leaving the ovaries. Mother and child made a good recovery, and were discharged from the hospital on the twenty-eighth day. On examining the specimen it was found that half of the old scar had ruptured. The other half remained firm through its entire thickness, and could be recognized by fine white lines in the serous covering of the uterus. It was found that the posterior portion of the scar remained intact, while the anterior half upon the fundus had ruptured. On examining the specimen closely the muscle fibers had fully reformed and showed a perfectly normal structure. The serosa could be detected, and at the point where the scar had been the inferior surface of the

scar showed healthy mucous membrane. In that portion of the scar which had ruptured the appearances were different. There was an abundance of old granulation cells, connective tissue, and decidual cells had largely taken the place of muscle fibres, while the mucous membrane of the uterus had developed upon the interior surface. Between the imperfect muscle bundles there was an appearance of connective tissue. On examining the records it was found that after the first section this patient had fever on the eighth day. At that time infection must have developed through the portion of the uterine wound which afterward ruptured, and this infection prevented the formation of the normal scar. In the last thirty years in Bumm's clinic there have been 3 ruptures of the uterine scar following Cesarean section. In the first, the wound in the fundus of the uterus was closed with silk. In the pregnancy which followed the operation rupture occurred during the ninth month. Abdominal section was at once performed, and the dead child removed from the abdominal cavity. The uterine wound had ruptured throughout its entire extent. Rupture of the scar occurred in the second case, two weeks before term, the patient having already had two Cesarean sections. In the second month of the third pregnancy the patient was operated upon for ventral hernia. The scar in the uterus was then examined and was apparently normal. Spontaneous rupture occurred, however.

The Disinfection of the Hands.—SCHAEFFER (*Zeitsch. f. Geburts. u. Gynäk.*, 1912, Band lxxi, Heft 2) reviews the various methods of disinfecting the hands, and narrates his experience in the Berlin Polyclinic, which caused him to believe that it was not so much a question of the antiseptic employed as it was thorough application to the hands and of mechanical cleansing. Alcohol is considered valuable in its usual form; or acetone, whose mechanical effect is excellent.

GYNECOLOGY

UNDER THE CHARGE OF

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Vaccine Diagnosis of Gonorrhea.—The results of a series of experiments, on a rather small number of patients, with the commercial vaccine "Arthigon" are reported by NEU (*Monatsschr. f. Geb. u. Gyn.*, 1913, xxxviii, 182). This is a gonococcus vaccine, supposed to contain 20,000,000 dead organisms to each cubic centimeter. Neu says that he was induced to undertake this work on account of the exaggeratedly enthusiastic reports that have been appearing in the literature concerning the absolute specificity of various reactions elicited by gonococcus vaccines, and the resulting certainty of establishing a diagnosis in this manner. Although his series comprises but 14 cases of certain,

3 of probable gonorrheal infection, and 9 of adnexal disease of doubtful etiology, these small numbers are more or less compensated for by the fact that all the cases were most carefully studied, being under constant observation in the ward during the entire treatment. Neu has found the local reaction—that produced at the site of injection—very uncertain and altogether unreliable; it can be slight in patients with a definite gonorrheal infection, and strong in those who have never had gonorrhea. The focal reaction—that occurring at the site of the disease—was practically never lacking in patients who reacted in any way at all, but in a few women with perfectly healthy genital organs a "focal reaction" occurred; that is, injection of the vaccine was followed by pain and tenderness in the adnexal regions. A general reaction—manifested by a rise of temperature of 1° C. or more—was frequently present, and was at times very marked, but even this was by no means constant. Not the slightest relation could be discovered between the intensity of this temperature rise and any therapeutic effect, as has been claimed by several authors. As a result of these investigations, Neu says that he is very pessimistic with regard to the value of gonococcus vaccine either in the diagnosis or treatment of gonorrhea in the female, and does not believe that from the former standpoint it can be considered anything like as reliable as is Koch's old tuberculin in the diagnosis of tuberculosis. With regard to the therapeutic effect, he has not seen in any of his cases any permanent improvement which could be ascribed to the vaccine.

Serum Treatment of Anemia Secondary to Uterine Hemorrhage.—Zubrzycki and Wolfsgruber (*Wien. klin. Woch.*, 1913, xxvi, 95) have tried intramuscular injections of defibrinated human blood serum in 6 cases of high grade anemia consequent upon uterine hemorrhages. One of the patients was suffering from cervical carcinoma, the others from conditions diagnosticated as metropathia hemorrhagica, endometritis, etc. In all cases a marked increase in the red-cell count was observed, together with improvement in the general condition, this rise in the blood count occurring so regularly after the institution of treatment that Zubrzycki and Wolfsgruber have no doubt as to their causal relationship. (It should be noted, however, that in all cases some other method of treatment was combined with the injections—*x*-ray applications in 2, curettement in 2, excochleation and paquelinization in 1, hysterectomy in 1. The method employed was to obtain blood from healthy waiting women in the obstetrical wards (Wassermann in each case negative), to defibrinate this by shaking with glass beads, and then to inject from 20 to 30 c.c. of the serum into the gluteal region of the patient. From two to five injections were given, no pain or unpleasant sequelæ of any sort being seen. Nothing is said as to any permanent effect in preventing recurrence of the hemorrhage.

Dysmenorrhea.—"Health is a perfect balance of the hormones; there are probably as many hormones as glands of internal secretion—indeed, our conception of the hormones can be expanded to consider that every organ has its specific hormone, that is, its specific metabolic product, which is poured into the general circulation." Starting from this hypothesis, Klein (*Monatsschr. f. Geb. u. Gyn.*, 1913, xxxvii,

169) says that he believes many cases of dysmenorrhea are due to an insufficient loss of coagulability on the part of the menstrual blood, the result of a hyposecretion of the ovarian hormone, which he terms oöphorine, and which has been demonstrated to have an antithrombic action on the menstrual blood. On the other hand, excessive secretion of oöphorine can also cause dysmenorrhea by producing an increased swelling of the endometrium, and hence secondary colics. This type of dysmenorrhea Klein has attempted to influence therapeutically by the employment of a hormone *antagonistic* in action to oöphorine, selecting for this purpose adrenalin, since it has a vasoconstrictor action, as opposed to the vasodilator action of oöphorine. He has tried this on 35 patients in whom he considered the dysmenorrhea to be the result of endometrial congestion consequent upon hypersecretion of the ovarian hormone, with very good results in all but two. He gives exceedingly small doses of adrenalin—0.1 to 0.5 milligram—subcutaneously or by mouth. In most instances, the cramps of which the patients complained were promptly relieved, and did not recur during the remainder of the menstrual period; indeed, in a few instances, the beneficial effect appeared to continue through the next following period as well. Klein states that he considers this work purely experimental as yet, but thinks that it represents an attempt to attack the problem along biologic lines, and hence that it may lead to the discovery of a truly causal therapy.

Vulvovaginitis in Children.—Rubin and Leopold (*Amer. Jour. Dis. of Children*, 1913, v, 58) report the results of a series of investigations into the cause of the persistence of gonorrheal vulvovaginitis in young children, these investigations having been carried out upon 50 patients, all of whom were under their observation for a considerable length of time. In order to determine the relative frequency of involvement of the cervix, Rubin and Leopold have employed routinely the electrically lighted female urethroscope, using in each instance an instrument adapted to the size and age of the child. Their technique is to place the patient in the dorsal position, and then to introduce the tube, with the obdurator in place, as far as it will go; the obdurator is then removed, and the tube gradually withdrawn until one of the cervical lips is encountered, when the entire cervix can generally be manipulated into the end of the instrument, and studied by direct examination. If the proper sized instrument is used, this procedure should not cause trauma, pain, or hemorrhage. The value of this method of examination is shown by the fact in the majority of patients the cervix was found to bear the brunt of the infection. The vagina also was found constantly affected, the appearance varying from a general or scattered congestion to the occurrence of small hemorrhagic areas, and even small ulcerations. Occasionally small pockets, containing a drop of pus, were seen and in some instances associated with these were adhesions near the vaginal vault. The chief lesions noted in the cervix consisted of depressions or lobulations, sometimes associated with ectropion of the cervical mucosa, resembling the erosions seen in adults. Mucus or muco-pus was often seen in the crypts, between the folds, and covering a greater or lesser portion of the orifice; in some instances, muco-pus could be seen escaping from the external os after

wiping off the vaginal surface. The evidence furnished by these findings is so definite that the authors say they are able to make a positive diagnosis as to the presence or absence of gonorrheal infection in young children by means of direct inspection through the urethroscope, without resorting to smears or cultures. With regard to treatment, Rubin and Leopold are extremely pessimistic. The subjects of their investigations have been treated for three years with all the known therapeutic measures—irrigations, ointments, yeast, vaccines, sera—without any appreciable benefit. They suggest, therefore, the necessity of adopting in these cases a more active therapy, similar in a general way to that applied to the treatment of gonorrhea in adults, but consider that before beginning this the extent of the deep lesion should in every instance be accurately determined by the use of the urethroscope, the appropriate medication being carried out by means of the same instrument.

Unusual Duplication of the Genito-urinary Tract.—A most remarkable case of this condition, which in view of its extent of development must certainly be considered unique in medical literature, is reported by GEMMEL and PATERSON (*Jour. Obst. and Gyn. Brit. Emp.*, 913, xxiii, 25). The subject of the report, a healthy, married woman, aged thirty-two years, presents the following abnormalities: The anterior-superior spinous processes are 11 inches apart, and there is no symphysis pubis, a gap of $5\frac{7}{8}$ inches existing between the pubic bones. The interval between the thighs forms a perineal space 4 inches in diameter; in this are two distinct vulvar orifices, side by side, about 3 inches apart, with a single anus behind the left vulva. The vulvæ are about normal in size and form, each with well developed labia majora and minora, a clitoris, urethral, and vaginal openings. The median labia majora on each side, however, are somewhat less prominent than the lateral. Each vagina easily admits two fingers; bimanual examination reveals the presence on each side of a well formed cervix and uterus, each of which can be freely moved independently of the other. A single ovary can be be felt at the outer side of each uterus. The urethræ appear normal; by catheterization 6 ounces of clear urine were obtained from the left urethra, 4 ounces of turbid urine, containing pus, from the right. By means of collargol injections through the urethræ, two distinct and separate bladders were demonstrated by the *x*-rays. Between and somewhat anterior to the two vulvæ is an area of skin, devoid of both hair and sweat glands. On palpation this area is found to correspond to a circular opening about $1\frac{1}{2}$ inches in diameter in the abdominal fascia; through this the abdominal viscera can be felt immediately beneath the thin skin. Gemmel and Paterson consider that this area represents the umbilicus, nothing else suggestive of that structure being present. One of the most interesting features about the case is that in 1910 pregnancy occurred in the right uterus, and the patient gave birth to a living male child through the right vagina; in 1912 pregnancy occurred in the left uterus, a living female child being delivered through the birth canal of that side. Both children were somewhat under-sized, but appeared to be about full term. Gemmel and Paterson ascribe all the anomalies to one underlying cause—the absence of an allantois,

and discuss the embryological features of the case at some length. Evidently there has been no median ventral diverticulum from the internal cloaca; the Müllerian ducts have remained separate, and have been drawn backward to the surface of the body, so that they have come to open separately on the surface of the cloaca before the time of differentiation of the external organs. Each Müllerian duct has then become separately differentiated into a vagina, uterus, and Fallopian tube. As a result of the lack of allantois, the pelvic girdle, although fully formed, has been arrested in development, and no symphysis pubis or mons veneris has been developed. No normal bladder has been produced, and the traction of the amnion, which must have enfolded the embryo and come in direct contact with the chorion and placenta, had favored separate connection of the Müllerian ducts with the external cloaca and the formation of bilateral bladders and urethræ out of the ventral portion of the internal cloaca. The umbilical orifice has remained patent, and a pseudoumbilicus has been formed by ligation of the body wall at the time of birth.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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Fundus Changes in Leukemia.—Hudson (*Royal London Ophthal. Hosp. Report*, September, 1911, p. 153) thus summarizes the present state of knowledge with regard to leukemia: Changes are met with in both lymphatic and myelogenous leukemia, and in both chronic and acute cases; they are, however, by no means constant, being found, according to Leber, in only one-third or one-quarter of all cases. Both eyes are almost always affected but not always in equal degree. The changes are in some cases limited to the appearance of scattered hemorrhages, while pre-retinal hemorrhage may also occur (Stock); in other cases, however, more characteristic features are present, consisting in a light yellowish hue of the whole eye ground; distension and tortuosity of the retinal vessels, affecting more especially the veins, which are of rose tint, while the blood stream in the arteries is abnormally pale; pallor and indistinctness of the optic disk, with a diffuse haze, involving the whole retina, and often more pronounced in the course of the main veins. The veins may be bordered by white bands, while hemorrhages are found scattered through the retina, together with white spots which, according to many authors, are more numerous in the periphery of the fundus, so that they may be invisible to ophthalmoscopic examination. Such spots are also met with in the macula; they are not infrequently surrounded by a red border, and

may exhibit a definite prominence. Movement of the blood stream in the veins has been observed ophthalmoscopically. It would seem that in the acute cases fundus changes of hemorrhagic and edematous origin tend to dominate the picture, while the more characteristic fundus changes have, for the most part, been observed in chronic cases.

Paralysis of the Accommodation after Diphtheria.—Oloff (*Klin. Monatsbl. f. Augenheilk.*, May, 1912, p. 551) observed paralysis of the accommodation, complete in the left eye and nearly so in the right, four years after a mild attack of diphtheria in a healthy young subject. No paralyses of other parts had been present. The pupillary action was preserved. Post-diphtheritic paralysis of the accommodation of six months duration and longer is extremely rare, perhaps not half a dozen cases are on record. Most authorities consider hypermetropia as a predisposing cause, in that it contributes to the strain of the weakened ciliary muscle during convalescence, which period is frequently spent in reading or other close work. Hypermetropia was not present in Oloff's case; in fact, one eye was emmetropic, and the other presented a low degree of simple myopic astigmatism. Opinions differ greatly as to the site of the lesion in this form of paralysis of the accommodation. Bumke, based upon the researches of Saenger and Wilbrand and of Nonne, thinks that the oculomotor nerve is at fault. Roemer and Stein locate the disturbance, as is the case in botulismus poison, in the small-celled median nucleus, the supposed centre of accommodation. They base their views upon the conclusions of Ehrlich regarding the poison of diphtheria. According to the latter authority, the bacillus elaborates two different substances; the one, the true toxin, cuses the symptoms of diphtheria proper in the fauces, while with the other, the toxon, he succeeded in producing paralyses experimentally. The action of the latter is much slower than that of the former. Roemer thinks that this view is supported by the relative inefficiency of the serum against paralyses, the effect of which is directed against the toxin rather than the toxon. This accounts for the fact that paralysis of the accommodation is observed as frequently at present as before the administration of the serum.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Nematodes as a Factor in the Production of Cancer.—Fibiger, of Copenhagen (*Berl. klin. Woch.*, February 17, 1913), shows some very interesting discoveries in the part played by nematodes in the causa-

tion of cancer in rats. First, his curiosity was aroused by finding three rats in the same cage affected by malignant growth of the stomach; this tumor, however, could not be grafted upon other rats. In the preparations, Fibiger saw oval holes and masses which suggested parasite bodies containing eggs. By serial sections, he found these actually were parasites, evidently a nematode; and casting about for the intermediate host, he performed 1144 autopsies on rats without definite results; he found, however, that one form of cockroach, *Periplaneta orientalis*, is the intermediate host of a filaria which is found in the rat's stomach; rats, however, fed on *P. orientalis* gave no results. Having traced his original three rats to Dorpat in Russia, he found that a sugar-refinery there was infected with *P. americana*, another variety of cockrach. Rats from the sugar refinery showed the changes so faithfully sought. Of 61 rats, 21 were negative, but 40 showed nematodes, while 18 of the 40 were affected by tumor growth, in 9 of which advanced growth like that in the original three rats was found. By feeding *P. americana* to labortary rats, 36 out of 57 positive results were obtained. *P. orientalis* was now infected by the nematodes from *P. americana*, and now the rats fed on the former showed the same positive results. Control rats fed on control non-infected cockroaches remained free from growths. The nematode is of the genus spiroptera, and has apparently not been previously described. Professor Fibiger's work is a wonderful example of close reasoning and painstaking work, and it has resulted in the production of experimental newgrowths, the first method which had definitely succeeded if one except their production, unintentionally by the *x*-rays.

Distemper in Dogs.—The causative organism of this disease may now be considered to be definitely known: It is the bacillus bronchisepticus of Ferry, an organism discovered at about the same time by Ferry, by McGowan, and by Torrey and Rahe, independently of one another. Extensive experiments by the last two workers, TORREY and RAHE (*Jour. Med. Research*, January, 1913) have given a large mass of accurate information. The organism is a small, slender, often paired bacillus, actively motile. In 90 cases, of the disease, they succeeded in finding bacillus in 75 per cent. It is found in the following organs, stated in the order of greatest frequency: Trachea, bronchi, lungs, nose, liver, brain, spleen, kidney, and blood. Secondary infections by other bacteria occur with great frequency. All the individual forms isolated fall within one species, as determined by agglutination tests, but one strain reduces nitrates, the other does not. The bacillus forms an endotoxin, but no exotoxins: nevertheless sterile filtrates of liquid cultures contain a free toxin, and attempts to prepare an antiserum were made by injecting toxin filtrate and bacteria, although the serum obtained a high agglutinative power it exerted no protective action. While McGowan failed to find a constant agglutinative power, Torrey and Rahe here quoted agree with Ferry in the contrary contention. The incubation period varies between four and fifteen days. The dried bacillus may remain viable for several months, but the infectivity of dried bacilli decreases rapidly, and in twenty days is lost. Susceptible dogs, actively immunized by subcutaneous injections of small doses of the bacillus, are immune to natural distemper.

Destruction of Leukocytes in the Blood Count by Thoma's Method.—MANUCHIN (*Russki Wratsch*, 1912, No. 5, S. 151) is responsible for the statement that as a result of the use of 0.3 per cent. acetic acid solution as used in Thoma's method 10 to 20 per cent. of the leukocytes present are destroyed.

Pseudotuberculosis in Man.—SAISAWA, of Tokio (*Zeitsch. f. Hyg. und Infektionskrankheiten*, 1913, lxxiii, Heft 3), describes a well observed case of pseudotuberculosis which happened in a soldier, was carefully noted throughout its course, and yielded complete bacteriological material. Before giving any particulars of Saisawa's case, it may be said that bacillary pseudotuberculosis is an infrequent disease, and few of the hitherto described cases have been given with sufficient fullness. Pseudotuberculosis is a disease most frequently of rodents, but it has been observed in mankind under the name of Zoögleic tuberculosis, and is not a clinical entity. It is caused by non-bacterial parasites such as blastomyces, actinomyces, the aspergillus group, certain protozoa, and even more highly developed organisms. Saisawa's case was caused by bacilli which were not acid fast, and correspond to the so-called "Pfeiffer pseudotuberculosis bacillus of rodents." The illness consisted of a fever with marked prostration, ending in death after ten days. There were icterus, enlargement of the liver and spleen, albumin and bile pigments in the urine, a moderate leukocytosis, in fine, a course not unlike that of typhoid fever. Blood cultures the day before death gave growths of the organism referred to above. At autopsy the most marked changes were observed in the intestines where the mucosa was swollen, slimy, and showed marked catarrhal places; there were hemorrhagic spots, Peyer's patches and the solitary follicles were greatly enlarged, and in one place there was an ulceration on the surface which lacked the appearances so characteristic of advanced tuberculous ulceration. The anatomical diagnosis gave follicular enteritis, tubercle formation in the liver and the spleen, edema of the lungs, nephritis, serous exudate in the peritoneum, pleuræ, and pericardium. The tubercles described in the liver and the spleen answer the description of the ordinary tubercle, each having a necrotic altered centre at the periphery of which small clumps of bacilli could sometimes be seen, but the bacillus tuberculosis could not be demonstrated in it. Briefly the bacilli obtained from the autopsy were the same as those obtained by blood cultures during life, and conformed to the organism above mentioned, which bears Pfeiffer's name. Saisawa carried out a very full set of observations upon various rodents, as well as upon the morphology of the organism. There has been much discussion as to the mode of infection in such cases, and Saisawa's offers arguments in favor of infection through the alimentary canal. Following this paper, Saisawa has carried out a series of experiments upon the bacillus pseudotuberculosis, he having obtained bacilli from four different sources in Europe. The five forms showed no important differences in morphology or cultivation; all are intensely pathogenic for rodents, causing a disease of an acute course with marked swelling and hyperemia of spleen, liver, and mesenteric glands, and the formation of tubercles in most of the organs. The serum reaction, agglutination, precipitation, and complement

fixation, gave unreliable results, so that these reactions offered little assistance in the identification of the different strains. One of the five stains, however, did give undoubted immunity against subsequent infections by the same, and the other forms. These bacilli are pleomorphic, usually bacillary, but sometimes coccal in form, often in diploform as well as in chains; they are non-motile, negative to Gram, stained with Loeffler's blue or carbol fuchsin show polar staining, and they grow at both room and body temperature.

The Ophthalmic Test in Glanders.—K. F. MEYER (*Jour. Infectious Diseases*, March, 1913) publishes his results in the employment of mallein dropped on the conjunctiva, as a test for the presence of glanders; this paper contains the facts regarding about 600 horses. A tested mallein preparation (in this case a 5 per cent. solution freshly made, of *mallein siccum* of Foth) is used, and 2 or 3 drops dropped on the conjunctiva of the horse to be tested. In ten and twenty-four hours, examination of the eye shows either no reaction at all, or a slimy discharge which is not counted a positive reaction, or a purulent discharge which is the requisite without which no reaction may be stated to have occurred. Should a reaction fail it is a great advantage that one may test in the same way after twenty or twenty-four hours more have elapsed. The plan offers a very useful weapon to the practising veterinarian for the detection of glanders, but is not intended to take the place of the complement fixation and agglutination tests, although present indications make it appear that it is more accurate than either one. When the serum tests are to be used, it is to be remembered that subcutaneous mallein test should be made previously.

What is the Least Lung Capacity Compatible with Life?—BERNARD, LE PLAY, and MANTOUX (*Jour. de Phys. et de Path. Gén.*, January 15, 1913, Vol. xv, No. 1) have sought to establish for the lungs the minimal capactiy which is capable of sustaining life. Courmount has found that ablation of three-quarter of the lung tissue left enough to support life, but the present writers have utilized the method of producing artificial pneumothorax by nitrogen. After complete anesthesia of a dog the collapse was produced as in the human subject, with control of the amount of gas used and observation of the state of the lung by radioscopy. Briefly, they found that the lung capacity could be reduced to one-sixth and life still be supported without knowing that this is exactly true for mankind. It nevertheless encourages us to suppose that a total collapse of one lung may be produced even if the other lung be partly affected by previous disease.

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